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**Boosting cognitive training
exploring Cognitive Bias Modification adaptations for adolescent anxiety**

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Boosting Cognitive Training: Exploring Cognitive Bias Modification adaptations for adolescent anxiety

Stephen C Lisk

King's College London

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Abstract

Anxiety disorders are one of the most prevalent mental health problems for adolescents. Cognitive Bias Modification (CBM) training targets information processing biases implicated in the development and maintenance of anxiety in adolescents. The main aim of this thesis is the development and evaluation of methods to boost CBM for anxious adolescents. The thesis first presents findings from a meta-analytic evaluation of eye-tracking studies in anxious children and adolescents; the results demonstrating no difference in vigilance to threat between anxious and non-anxious youth, but a greater overall avoidance of threat in anxious youth. Following this, three experimental studies are presented, evaluating methods to boost CBM in anxious adolescents. The first evaluates a multi-session, combined bias CBM package, targeting biases of attention, interpretation and attribution in socially anxious adolescents. Results demonstrate good acceptability and greater reductions in social anxiety, negative social behaviour, general anxiety and depression following an intervention but not a baseline phase, and a significant correlation between interpretation bias change and social anxiety symptom change. The second experimental study aims to boost attention bias modification by comparing incorporation of an extrinsic motivator, in the form of real-time performance feedback, and the use of real-time performance data to tailor the task to the individuals' optimal rate of learning. Results show an overall modification of attention bias on one measure of attention bias, which did not generalise to an alternative measure, and an effect of initial direction of attention bias on modification outcome. However, no differential effect of training group was observed. The final experiment evaluated the use of neurofeedback (NF), which aims to boost the practice of adaptive emotion regulation strategies by providing real-time feedback of activity from associated brain regions in adolescents. Results showed that individuals unable to acquire the desired pattern of connectivity through NF training displayed greater subsequent social-avoidant behaviour than

those who successfully acquired the desired connectivity pattern, as well as reporting a significant decrease in reappraisal ability. The findings are discussed in the context of the wider literature, providing implications for theory and future directions.

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Statement of Authorship

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Chapters two, three and four were led by myself from design to completion, along with advice and input from my supervisor. I was solely responsible for creation of experimental tasks, participant recruitment, collection of data, analysis and write-up. During the meta-analysis in chapter two, two other lab members assisted to validate literature search results and coding of study variables. Data from chapter five was collected at Oxford University as part of a larger neurofeedback study, carried out in collaboration with the BrainTrain consortium. I was involved in study design and collected data for twenty-five participants. Other than processing of the fMRI data by a postgraduate researcher, I was solely responsible for statistical analysis of all data appearing in chapter five. All work in the thesis is original and the result of my own work.

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Chapter 1

1

Introduction

1.1 Introduction and overview

Anxiety is the most common mental health condition in children and adolescents (Essau & Gabbidon, 2013). It was recently estimated that anxiety affects 6.5% of young people globally (Polanczyk, Salum, Sugaya, Caye, & Rohde, 2015). To put this into context, this suggests anxiety disorders affect approximately 117 million young people worldwide at a single time point. This is perhaps even more important when acknowledging that untreated anxiety in younger years is associated with later mental health problems (Pine, Cohen, Gurley, Brook, & Ma, 1998; Woodward & Fergusson, 2001). In fact, even with a diagnosis, an anxiety disorder in childhood and adolescence is the most common predictor of anxiety and depression in adulthood (Kim-Cohen et al., 2003) – this is perhaps less surprising when learning that children and adolescents diagnosed with anxiety problems commonly remain untreated (Essau, 2005). Despite these considerable problems and poor prognosis, child and adolescent anxiety is still a surprisingly neglected area of research. Cognitive models of anxiety implicate biased processing of threat-relevant information in the maintenance and development of anxiety symptoms (Eysenck, 2003). Theoretical advancement of these models has led to the development of cognitive experimental tasks designed to measure and modify these anxiety-linked cognitive processes. This chapter will begin with an overview of the classification, diagnosis and epidemiology of anxiety disorders in young people, before outlining cognitive theoretical accounts of anxiety. This will be followed by an overview of the literature surrounding measurement and modification of cognitive biases in young people. Finally, the main aims of the current thesis will be outlined.

1.2. Anxiety

1.2.1 What is anxiety?

Anxiety is an adaptive emotional response to threat, either actual or potential (Craske et al., 2011). Much of the time it is a transient response that can act as a functional tool for well-being or survival. However, when these responses are irrational and disproportionate to the severity of threat, they can significantly interfere in mental wellbeing and daily functioning (Mendlowicz & Stein, 2000). As such, anxiety disorders can be incredibly debilitating to quality of life and have detrimental long-term consequences (Mendlowicz & Stein, 2000). Pathological anxiety may manifest itself in a constellation of behavioural (e.g. irrational avoidance and withdrawal from situations which have previously resulted in anxiety), physiological (e.g. increased heart rate, fatigue, restlessness, muscular tension), and cognitive (e.g. uncontrollable worry, fears of losing control, difficulty concentrating, general expectation of future threat) symptoms.

Anxiety can be conceptualised categorically or dimensionally. The categorical view conceptualises anxiety as multiple separate sub-disorders, each identified by the presence of specific symptoms occurring over a prolonged period of time. These clusters of symptoms must be present together, differentiate from normative (developmentally appropriate) fears, and continue for a defined period of time in order for the associated disorder to be diagnosed. Classification and diagnosis in this manner rely upon diagnostic manuals that have been created and are periodically updated based on clinical evidence. The two major psychiatric manuals used to classify anxiety disorders in all ages are the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013), and the International Statistical Classification of Diseases and Related Health Problems (ICD-10; World Health Organization, 1993). DSM-5 outlines seven subsections of anxiety, six of which are presented in Table 1.1 along with common symptoms associated with each. For

instance, according to DSM-5, social anxiety disorder in youth can be summarised as a persistent and disproportionate fear of one or more social or performance situations that involves possible scrutiny by others, in which there is also significant avoidance of the feared situation, and evidence the young person is able to have age-appropriate relationships. Furthermore, these symptoms must be regularly present for six or more months. Thus, a clear set of conditions that must all be apparent for a prolonged period for the specific disorder to be “present”. Alternatively, it can be strongly argued that this categorical view oversimplifies the complexity of symptoms, and underestimates individual differences in symptoms within and across diagnostic boundaries (Beesdo, Knappe, & Pine, 2009; Jablensky 1999; Kendell & Jablensky, 2003). The alternative view proposes that anxiety symptoms can be conceptualised dimensionally, where characteristics vary along a continuum and impairing symptoms can be understood as extreme variants of normative traits. There is evidence to support this view, with the profile and severity of symptoms in anxiety disorders shown to vary continuously across individuals in both clinical and community settings (Stein et al., 2010). Furthermore, evidence suggests those at a sub-threshold level of anxiety still show significant impairment in functioning and a vulnerability to more severe symptoms over time (Balázs et al., 2013).

Thus, dimensional ratings allow for a more specific conceptualisation of symptom profiles, however categorical approaches are still essential tools to facilitate clinical and research communication. As such, anxiety disorders can be viewed from both angles, and these approaches are often employed in tandem; DSM-5 now acknowledges the dimensional aspect of symptoms and has taken modest steps towards incorporating shared dimensions and measures indicating degree of acuteness; however, disorders remain in specific categories. In research and clinical fields, dimensional questionnaire measures are often used to assess the natural variation in individual symptoms along a continuum but also identify individuals that fall in the “elevated” or “clinical” thresholds for a specific disorder.

Table 1.1. Categories of anxiety disorders and associated symptoms

Anxiety disorder	Definition
Agoraphobia	Intense fear (and avoidance) of being in a situation or place that does not allow for easy exit or escape; or where escape may cause embarrassment; or where help may not be available in the result of an adverse reaction, such as having a panic attack. Common examples include public transport, being alone outside of home.
Generalised Anxiety Disorder	Excessive anxiety / uncontrollable worry about possibility of negative outcomes across various aspects of life – though often regarding school performance in young people. Level of worry is disproportionate to the feared outcome. Typically, overzealous in their search of reassurance and approval. They may also be overly conforming and perfectionist.
Panic Disorder	Surge of intense anxiety, with accompanying physiological symptoms (heart palpitations, sweating, shaking, shortness of breath, dizziness). Compared to adults, children and adolescents may more often display behaviours such as screaming or crying.
Separation Anxiety Disorder	Anxiety regarding separation from home or attachment figures. Often expressed as persistent fear of danger to the attachment figure when separated, and symptoms such as dizziness, stomach-aches or headaches in anticipation of separation. These exceed behaviours expected for the developmental age.
Social Anxiety Disorder (formerly social phobia)	Fear of negative social evaluation. Fear of humiliation or embarrassment in social or performance situations. Exposure to these situations leads to an anxious response. Often results in behavioural avoidance of feared situations.
Specific Phobia	Disproportionate level of anxiety associated with a specific event or object (e.g. spider, needles). Often manifests itself in avoidance of the feared stimulus, fearful anticipation, or extreme anxiety during the encounter.

Selective mutism has been classified as an anxiety disorder within DSM-5, however as there has been little research of this disorder in relation to the theme of this thesis, it is not included in this table.

1.2.2. Measurement and diagnosis

For categorical assessment of anxiety disorders, clinical interviews are considered the gold standard. The most commonly used form of interview is the semi-structured interview, in which a clinician assesses the individual against specified criteria outlined in DSM-5 or ICD-10, with flexibility to follow up on responses in order to accurately arrive at the resultant presence or absence of a diagnosis. The most widely used interview for young people with anxiety is the Anxiety Disorders Interview Schedule for Children and Parents (ADIS-C/P; Silverman & Albano, 1996), which provides questions for symptoms, time-course of problems, cognitive and situational factors, as well as information for comorbid diagnoses. Other semi-structured interviews that take a similar approach are: Schedule for Affective Disorders and Schizophrenia for School-Age Children (KSADS; Kaufman, Birmaher, Brent, Rao, & Ryan, 1996); Diagnostic Interview for Children and Adolescents (DICA; Reich, 2000); Child and Adolescent Psychiatry Assessment (CAPA; Angold, Prendergast, Cox, Harrington, Simonoff, & Rutter, 1995); Child Assessment Schedule (CAS; Hodges et al., 1982); Children's Anxiety Evaluation Form (CAEF; Hoehn-Saric, Maisami, & Wiegand, 1987).

Questionnaire measures are used to assess variations of anxiety at symptom level. These measures of anxiety can produce overall anxiety scores but often include sub-scales, based on items assessing specific symptom dimensions. Typically, each questionnaire will consist of questions or statements regarding anxiety-related feelings or associated behaviour, with the respondent asked to indicate frequency or severity (e.g. "How often do you feel this way?", "how true is this statement for you?"). These measures can be used as a continuous measure of anxiety symptoms and transformed into a dichotomous outcome to estimate the likely clinical status (i.e. above a clinical or elevated threshold). It is important that questionnaires in use have high construct and criterion validity in order to generalise findings to the constructs defined by classification manuals. Some commonly used questionnaire

measures for child and adolescent anxiety include; the Screen for Childhood Anxiety Related Emotional Disorders (SCARED; Birmaher et al., 1997), the Revised Children's Anxiety and Depression Scale (RCADS; Chorpita, Ebesutani, & Spence, 2015), and the Spence Children's Anxiety Scale (SCAS; Spence, 1998) – these are free resources that have shown good reliability and validity (Donnelly et al., 2018; Hale, Raaijmakers, Muris, & Meeus, 2005; Spence, Barrett, & Turner, 2003). To specifically measure social anxiety in adolescence the Social Anxiety Scale for Adolescents (SAS-A; La Greca, & Lopez, 1998) is often used. This has the advantage of being constructed specifically for adolescents and has been demonstrated to be a developmentally appropriate instrument to examine social anxiety in adolescence through a process of validation (Nelemans, et al 2017). Other questionnaire measures used include; the Multidimensional Anxiety Scale for Children (MASC; March, 1997), the State-Trait Anxiety Inventory for Children (STAI-C; Spielberger, 1973), the Social Phobia and Anxiety Inventory for Children (SPAI-C; Beidel, Turner, & Morris, 1998), and the Revised Children's Manifest Anxiety Scale, (RCMAS; Reynolds & Richmond (1978).

1.2.3. Prevalence of anxiety in youth

Anxiety disorders have been shown as the most prevalent mental health issue for children and adolescents worldwide (Polanczyk et al., 2015), with average age of onset around 11 years (Kessler et al., 2007). Though estimates vary, a recent global meta-analysis including cross-sectional studies of mixed anxiety disorders gave a global point prevalence of 6.5% (Polanczyk et al 2015). A recent European study assessed around 12,000 adolescents and estimated an anxiety disorder prevalence of 5.8%, with prevalence of subthreshold anxiety rising to 32% (Balázs et al., 2013). Furthermore, estimates suggest between approximately 15% and 30% of children and adolescents have been diagnosed with an

anxiety disorder at some period of childhood and adolescence (Beesdo et al., 2009; Copeland, Angold, Shanahan, & Costello, 2014; Woodward & Fergusson, 2001).

Emergence and prevalence of specific anxiety disorders have been shown to vary across developmental timepoints. Specific phobias, separation anxiety disorder and social anxiety disorder are all most commonly diagnosed in childhood and adolescence. Specific phobias and separation anxiety disorder are suggested to be the earliest anxiety disorders to emerge, at around seven to nine years of age (Kessler et al., 2012; Last, Perrin, Hersen, & Kazdin, 1992). Social anxiety disorder has been identified in children as young as eight (Beidel & Turner, 1998), however, evidence from longitudinal investigations suggests a robust increase in onset rates during the transition into adolescence (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Costello, et al., 2011). In fact, social anxiety disorder has been identified as a persistent problem across adolescence: along with specific phobias, social anxiety is the most common anxiety disorder in adolescence (Merikangas et al., 2010), with significantly more extreme forms of social anxiety emerging by mid-adolescence (Wittchen, Stein, & Kessler, 1999). Panic disorder and generalised anxiety disorder both show their mean age of onset in adulthood, however longitudinal studies have found middle adolescence does show a modest increase in these disorders (Costello et al., 2003).

1.2.4. Impact of anxiety in youth

Anxiety in young people is associated with significant impairments to quality of life; across childhood and adolescence it has been shown to significantly disrupt academic performance and impair interpersonal interactions (Owens, Stevenson, Norgate, & Hadwin, 2008). Furthermore, longitudinal designs have provided substantial evidence for prolonged experience of anxiety across the life-course. Evidence suggests significant ‘homotypic continuity’, meaning young people with an anxiety disorder are likely to experience that disorder again subsequently in the course of their life (Pine et al., 1998; Woodward &

Fergusson, 2001). They are also at significant risk of developing another form of psychopathology, with heterotypic continuity from anxiety to depression consistently demonstrated (Costello et al., 2003; Pine, Cohen, & Brook, 2001; Pine et al., 1998) but also from anxiety to substance abuse in mid-adolescence (Costello et al., 2003; Crum & Pratt, 2001). Thus, child and adolescent anxiety can be an enduring issue following onset; one that has the ability to affect an individual throughout their life, as well as a risk factor for developing other disorders. Anxiety disorders have also been found to consistently co-occur with other disorders in young people, particularly depression (Beesdo et al., 2009; Ford et al., 2003; Lewinsohn, Zinbarg, Seeley, Lewinsohn, & Sack, 1997), and other anxiety disorders (Esbjorn et al., 2010; Ford et al., 2003).

1.2.4. Current treatment options (and accessibility)

There is some evidence that the use of medication can be effective in the treatment of child and adolescent anxiety disorders. Selective serotonin reuptake inhibitors (SSRIs) are the favoured medication due to their safety profile compared to other choices, such as benzodiazepines, and a recent meta-analysis found SSRIs to show moderate effectiveness in treatment of anxiety disorders in youth (Kodish, Rockhill, Ryan, & Varley, 2011). However, the frontline treatment, and most frequently evaluated approaches, for child and adolescent anxiety disorders are psychological therapies. Cognitive Behavioural Therapy (CBT) in particular has the deepest evidence base for anxiety treatment in young people (James, James, Cowdrey, Soler, & Choke, 2013). CBT is a treatment model consisting of cognitive and behavioural interventions that aim to reduce symptoms by restructuring dysfunctional cognitions and decreasing maladaptive behaviours (Kendall, 2011). James et al (2013) conducted a review of 41 studies, finding that CBT was more effective (59% remission rate) than waitlist controls (19%); however, in studies using a non-CBT active control group (such as school support) there was no significant difference in outcome. Therefore, CBT

demonstrates effectiveness, but cannot be deemed the most effective treatment for youth anxiety.

Despite these continuing efforts to provide appropriate care and timely interventions, the majority of young people with an anxiety disorder do not receive treatment from a clinical service (Merikangas et al., 2011). Long waiting lists, lack of available services, a lack of awareness of treatment availability, and family issues are all thought to contribute (Care Quality Commission, 2017). Based on these issues, recent focus has been on development of more accessible front-line alternatives that are able to either provide a therapeutic option to those waiting for treatment, work adjunctively to boost ongoing treatment, or operate as an accessible standalone intervention option. There has been some success with remote/internet-based and parent-led forms of CBT (Cobham, 2012; Khanna & Kendall, 2010; March, Spence, & Donovan, 2008; Thirlwall et al., 2013), however further development of effective and accessible treatment options remains an important objective.

1.2.5. Adolescence: a crucial time for investigation and intervention?

Adolescence in particular may be a crucial time for research and intervention development. Cognitive neuroscience research suggests neurobiological changes during adolescence may facilitate the development of anxiety: connectivity between prefrontal cortex regions and areas of the limbic system, strongly implicated in emotion processing and regulation (Goldin, McRae, Ramel, & Gross, 2008), has been shown to develop significantly across adolescence (Ochsner, Bung, Gross, & Gabrieli, 2002; Nelson, Leibenluft, McClure, & Pine, 2005; Yurgelun-Todd, 2007). These developmental changes could mean greater variability between individuals – and it is possible that those with a greater risk for developing anxiety have poorer dysconnectivity in these emotion-processing circuits, which in turn influences the emergence of maladaptive cognitive strategies associated with anxiety symptoms. Protracted maturation of brain areas involved in emotion regulation (Casey, Jones,

& Hare, 2008), with possibly more experience-dependent pruning, may also mean that adolescence is a period of heightened plasticity. Consequently, adolescence may also be a critical time for intervention in anxiety disorders. The relative plasticity at this period of development may afford a greater responsiveness to positive interventions and, as such, present an opportune time to prevent the escalation of anxiety symptoms. In order to effectively intervene at this critical developmental juncture, research must continue to identify the processes which differentiate anxious from non-anxious individuals, and devise methods with which these processes can be most effectively targeted.

1.2.6. Summary

In summary, anxiety disorders are the most common mental health problems in children and adolescence, with varying prevalence across development. Child and adolescent anxiety disorders predict significant vulnerability for further anxiety problems, or impairment from another mental health disorder later in life. Separation anxiety and specific phobias appear to emerge earlier in childhood, whereas social anxiety disorder poses a particular problem in adolescence, with extreme and persistent forms of the disorder emerging by mid-adolescence. Cognitive behavioural approaches have the largest evidence base for treatment, however accessibility, cost, and ineffectiveness for some patients are challenges that need to be addressed. Providing easily-accessible treatments in adolescence could have a significant positive impact and seem essential to improving short and long-term outcomes for affected individuals. Therefore, the following sections will outline specific theories regarding cognitive influences on anxiety, before exploring evidence suggesting cognitive biases provide a direct intervention target for symptom reduction in anxious youth.

1.3. Cognitive models of anxiety

Anxiety has been explored in a multidisciplinary framework that includes genetic and environmental factors (Eley, 1999) interacting to influence cognitive and neurobiological risks (Mathew, Coplan, & Gorman, 2001). Whilst genetic and biological theories provide insightful and hugely important avenues for aetiological research, it can be suggested that these are somewhat more distal, and therefore less modifiable by cognitive behavioural techniques. Therefore, the current thesis will take a cognitive approach to anxiety.

Cognitive approaches to emotional disorders focus on individual differences in the processes we employ to select, interpret and remember information from our environment. A number of theorists have proposed a close link between cognition and emotion, suggesting distorted cognitions may play a crucial role in the maintenance of anxiety disorders (Beck, Emery, & Greenberg, 1985; Eysenck, 1992; Williams, Watts, MacLeod, & Mathews, 1997). Most notably, the early ideas of Beck (1976) have been particularly prominent in the development of cognitive approaches to understanding anxiety. His cognitive theory of emotion processing was first applied to depression (Beck, 1976), suggesting depressed individuals hold dysfunctional schemas; an overly negative set of beliefs and expectations about themselves focusing on themes of failure and loss. This theory was subsequently adapted to anxiety; in this case distorted schemas focused on threat and danger (Beck & Clark, 1988, 1997; Beck et al., 1985). Beck proposed chronic over-activation of these schemas results in processing resources being overly focused on threat-relevant information, expressed as cognitive distortions; negative automatic thoughts about the self, the environment and the future.

Taking schema-based cognitive models of anxiety developed for youth (Kendall et al., 1985) and applying these ideas within an information processing framework (Crick & Dodge, 1994) has resulted in the formulation of models detailing how selective processing of threat-based information may occur along several stages of information processing in anxious

young people (Daleiden & Vasey, 1997; Muris & Field, 2008; Williams, et al., 1988). Information is suggested to be processed through several stages (Crick & Dodge, 1994); a simplified overview suggests early detection and selection of information for encoding subsequent processing is followed by interpretation of the meaning of that information, and possible responses retrieved from memory or generated based on available social cues. In applying this approach to cognitive theories of anxiety it has been proposed that the anxious individual will be guided by maladaptive schemas that direct; selective *attention* to threatening information, threat-biased *interpretations* of ambiguous information, and selective *recall* of threatening information, all of which maintain the threat-focused thoughts and behaviours associated with anxiety disorders (Daleiden & Vasey, 1997; Muris & Field, 2008). Within each of these stages, automatic and strategic forms of processing are suggested to be involved: automatic processing is thought to operate outside conscious awareness and is driven by bottom-up mechanisms; these mechanisms are thought to function on sensory input, for example rapidly shifting attention to salient elements of a scene that hold potential importance. In contrast, strategic processing operates within conscious awareness and is suggested to be driven by controlled top-down mechanisms; i.e. mechanisms that execute longer-term, goal-directed cognitive strategies (Shiffrin & Schneider, 1977). Thus, anxiety is suggested to be characterised by biased automatic and/or strategic processing of threat-related information across the stages of attention, interpretation and memory, which maintain symptoms of anxiety. The following paragraphs will provide more detail as to the proposed role of attention and interpretation processing biases. Whilst all three listed above are suggested to play some role in youth anxiety symptoms (Rapee, Schniering, & Hudson, 2009), as memory biases are currently the least researched, the remainder of thesis will focus only on biases of attention and interpretation.

1.3.1. Attention

Selective attention biases refer to the preferential allocation of attention to emotionally-salient stimuli. Several experimental methods used to probe attention processes in adults show distinct patterns of biased attention allocation in relation to anxiety (Mogg & Bradley, 2016); however, there is some debate over the precise nature of the bias, with several prominent components of attention bias in anxiety having been proposed (Cisler & Koster, 2010). The first is *facilitated attention (vigilance)* for threat; this refers to how easily (or quickly) automatic attention is captured by threatening stimuli. It is suggested that anxious individuals are hypersensitive to threat, leading to more frequent and preferential automatic orienting of attention toward perceived threat than non-anxious individuals; it's suggested that this subsequently results in vulnerability to anxiety (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & Van Ijzendoorn, 2007; Williams, et al., 1988) and maintenance of anxiety symptoms. Secondly, some theories suggest that observed differences in attention bias may lie in *maintained attention* toward threat in anxious individuals, where anxious individuals dwell upon threatening stimuli following attentional capture. Fox et al (2001, 2002) propose that this maintained attention on threat is due to a *difficulty disengaging* from threat following attentional capture and may lead the individual to continue to 'ruminate' on threat-related outcomes and thus increase feelings of anxiety and/or prolong their anxious state. Finally, *avoidance* of threat is suggested to occur at later stages of attentional processing, with the individual directing voluntary attention away from the threatening stimuli to suppress feelings of anxiety, and in-turn preventing the opportunity to process information that may disconfirm irrational fears (Mogg, Bradley, Miles, & Dixon, 2004). The *vigilance-avoidance* hypothesis (Mogg et al., 2004) proposes a combination of these components across the time-course of attentional processing; it is suggested that, in anxious individuals, vigilance toward threat is followed by exaggerated top-down re-direction of attention away from threat. It is possible that these mechanisms may all play a role over

the time-course of attentional deployment (i.e. a mixture of bottom-up stimulus-driven mechanisms and top-down cognitive control mechanisms across attentional involvement).

1.3.2. Interpretation

Following attentional allocation and encoding, the next stage of processing is interpretation of the information. This stage is proposed to contain several facets (Daleiden & Vasey, 1997); i) appraising and attaching meaning to the information, ii) attributing causation, and iii) generating an expectation of the outcome. During this stage, cognitive models suggest anxious individuals display ‘schema-congruent’ biased interpretations of ambiguous or mildly negative cues. This biased appraisal style of assigning threatening meaning to often harmless situations and events elicits feelings of anxiety and fear, possibly strengthening the maladaptive schemas. Using several methods, research in adults has consistently found anxiety to be associated with both online (automatic) and offline (strategic) *interpretation* biases (Hirsch, Meeten, Krahé, & Reeder, 2016) – with anxiety thought to be linked with more threatening interpretations of ambiguous stimuli. There are now multiple studies showing a link between negative interpretations of ambiguous stimuli and anxiety (Hirsch et al., 2016; Stuijzand, Creswell, Field, Pearcey, & Dodd, 2018). During the process of *attribution*, it is proposed that anxious individuals are more likely to attribute causality to themselves for events they perceive as negative, such as failures or negative outcomes, compared to events they perceive as positive, such as successes (Hope, Gansler & Heimberg, 1989; Heimberg et al., 1989; Hope, Heimberg, Zollo, Nyman, & O’Brien, 1987).

1.3.3. Considering development

It is important to note that the proposed mechanisms of these biases are largely based upon evidence from adult studies. Whilst adult models assume these biases are fully formed, during developmental stages there may subtle or substantial differences in the nature of cognitive biases. Progressive development and consolidation of these processes may continue

through development, changing how they operate at various developmental junctures, and thus affecting how they should be intervened upon (Creswell & O'Connor, 2011; Dudeney, Sharpe, & Hunt, 2015; Field & Lester, 2010; Hadwin, Garner, & Perez-Olivas, 2006).

Therefore, as evidence from adult studies cannot be simply extrapolated to younger populations, developmental research is crucial to identify critical time periods concerning aberrant cognitive processing.

1.3.4. Summary

Information processing theories of anxiety in children and adolescents draw from adult theories, suggesting selective processing of threat-related information via attention, interpretation and memory all play a role in anxiety disorders. These processes may change or develop significantly during childhood and adolescence. The information processing approach to anxiety provides several important advantages; firstly, it provides a coherent structure from which to understand the processing of information in anxiety disordered individuals (Daleiden & Vasey, 1997). Secondly, the division of information processing into a logical sequence of events provides a systematic framework from which research can operate in order to build a more elaborate understanding of anxiety-linked processes, based on observable behaviour (MacLeod, 1993; Massaro & Cowan, 1993). Thirdly, the methods employed allow for the consideration of automatic, pre-conscious processes that cannot be measured with approaches such as self-report and are therefore not as susceptible to response bias. The next section will provide an overview of experimental tasks used to evaluate the presence and magnitude of cognitive biases in anxious individuals, before reviewing evidence for the presence of attention and interpretation biases in anxious children and adolescents, in addition to methods used to attempt modification of these biases in order to infer causality.

1.4. Measuring Anxiety-Related Cognitive Biases in Children and Adolescents:

Overview of methods and findings

1.4.1. Attention Bias

The following sections will provide an overview of the tasks used to measure attention biases in young people, and evidence for associations with anxiety symptoms in childhood and adolescence.

Tasks used to measure attention bias in children and adolescents

Most experimental measures of cognitive biases in young people represent extensions of those used successfully with adult participants. In general, attention biases are inferred from these tasks by comparing responses to threatening versus non-threatening stimuli. *The Emotional Stroop task* (Williams, Mathews, & MacLeod, 1996) presents age-appropriate words with varying threatening value (e.g. threatening & neutral) in different colours. Participants are instructed to ignore the meaning of the word and report the colour of the word as quickly as possible. Slower response times to report the colour of threatening words compared to neutral, indicate attentional capture by the content of the word. However, it is difficult to tell whether this task probes automatic attention-orienting towards a threat-valenced word, an inability to flexibly deploy attention away from emotional to non-emotional characteristics of the word, i.e. difficulty disengaging attention, or overt response biases that favour processing stimuli that is congruent with the mood-state. Other measures have therefore been developed too. Most commonly used is the dot probe task. *The dot probe task* (MacLeod, Mathews, & Tata, 1986) briefly exposes participants to a threatening and a neutral stimulus (e.g. age-appropriate words or faces) on a computer screen, for a set duration (e.g. 500ms). Subsequently, the stimuli disappear, and a probe appears in the location of either the threatening or neutral stimuli, with the participant's reaction time in identifying the

probe measured. Attentional biases toward threat are inferred from faster response times towards threat stimuli (congruent trials) than neutral stimuli (incongruent trials), though these may be due to biased orienting toward threat or delayed disengagement from threat. In attempts to assess the time-course of attention bias (investigating the vigilance-avoidance hypothesis), researchers have varied stimulus presentation times (e.g. 150ms, 500ms, 1200ms), with shorter durations (<500ms) thought to tap into automatic/involuntary attention, and longer presentation times (>500ms) designed to probe subsequent voluntary/strategic attention biases, hypothesised to be avoidant in nature (Mogg, Bradley, Miles, & Dixon, 2004). *The spatial cueing task* was developed as a method to assess threat disengagement; this task resembles the dot probe task but instead of presenting two competing stimuli for attention, only presents one stimulus (threat or neutral) that is replaced by a probe that is valid (in the same location) or invalid (different location). An advantage of the spatial cueing task is that it can differentiate between biased attentional-engagement of threat stimuli (comparing the valid threat and valid neutral trials) and biased attentional-disengagement of threat stimuli (comparing the invalid threat and invalid neutral trials). Despite this, the measure is infrequently used in children and adolescents. A final measure of spatial attentional allocation is the *Emotional Visual Search Task* (Ohman, Flykt, & Esteves, 2001), in which participants are shown a series of grids (e.g. 3 rows x 3 columns) of emotional faces. In each grid a target stimulus is embedded amongst several distractor stimuli. In some grids, they must select the positive stimuli (e.g. positive face) among the threatening stimuli (e.g. angry faces), and in other grids they must select the threat amongst the positive stimuli. Attention biases to threat are inferred from shorter mean reaction times to select the threatening stimuli than to select positive; due to the explicit instructions and the longer presentation time, it is possible this measure includes assessment of more voluntary/strategic processes.

Whilst all these measures of attention biases rely on the comparison of reaction times across conditions to infer attentional-focus, a more direct measure of overt attention is provided by the quantification of eye-gaze. *Eye-tracking tasks* (Armstrong & Olatunji, 2012) have recently been implemented together with free-viewing tasks, where threatening and neutral stimuli compete for attention. These designs allow for tracking of the individual's gaze across the entire time-course of stimulus presentation, during passive viewing, to provide a more proximal and continuous measure of attention than manual key presses. Frequently-used indices from eye-tracking studies include; *probability and latency of first fixations* to a particular stimuli, enabling an assessment of initial orienting responses toward threat; *initial maintenance*, where recording the length of each first fixation to threat allows researchers to obtain an index how readily threat maintains this initial fixation (i.e. difficulty disengaging initial attention from threat); *maintained attention*, where mean dwell time on threatening versus non-threatening stimuli is calculated over the entire trial, with a greater mean dwell time on threatening stimuli indicating overall maintained attention toward threat, and greater mean dwell time on non-threatening stimuli suggesting overall avoidance of threat; finally, taking advantage of the continuous measure of attention afforded by eye-tracking tasks, some studies have split total viewing time into time windows in an attempt to evaluate *vigilance-avoidance* patterns across the viewing period.

Evidence for attention bias in children and adolescents

The last two decades have reported over forty RT studies investigating attention biases in child and adolescent anxiety. The Stroop and the dot probe tasks have been popular measures of attentional bias in young people with anxiety, with much of the more recent literature favouring the use of the dot probe task. Studies of children and adolescents with a range of different anxiety disorders have reported results indicating a pattern of attention bias to threatening stimuli, using the Stroop task (Hadwin, Donnelly, Richards, French, & Patel

2009; Richards, Nash, Hadwin, & Donnelly, 2007; Taghavi, Dalglish, Moradi, Neshat-Doost, & Yule, 2003) and dot probe task (Dalglish et al., 2003; Eldar et al., 2012; Roy et al., 2008; Vasey, Daleiden, Williams, & Brown, 1995; Waters, Henry, Mogg, Bradley, & Pine, 2010). Associations between attention bias toward threat and anxiety severity have also been found in studies applying a dimensional approach to symptom measurement (Abend et al., 2018a; Telzer et al., 2008). However, using the dot probe task, there has also been evidence for associations between anxiety and attention bias away from threat (avoidance) (Brown et al., 2013; Monk et al., 2006; Stirling, Eley, & Clark 2006) during automatic stages of attention, and some studies finding no difference between anxious and non-anxious youth (Benoit, McNally, Rapee, Gamble & Wiseman, 2007; Britton et al., 2012; Hadwin, Donnelly, Richards, French & Patel, 2009). Although there is limited quantity of investigations into vigilance-avoidance patterns in the child and adolescent RT literature, there is some evidence for varying patterns of attention bias within studies that compare different presentation times (Salum et al., 2013; Waters, Bradley, & Mogg, 2014).

Therefore, across studies, there is a mixed pattern of findings in regard to anxiety-linked attention biases: while some studies have found a bias towards threat others have found an avoidance of threat, still others find no difference between anxious and non-anxious children and adolescents. It's possible these inconsistent findings are due to the inconsistency in methods across studies; bias measurement task choice and task parameters, such as presentation time or emotional stimulus, all vary across studies, as do anxiety diagnoses. A recent meta-analysis (Dudeney et al., 2015) served to clarify some of these findings by pooling together results of thirty-eight attention bias studies in anxious children and adolescents and conducting moderator analyses for these heterogenous factors. Overall a greater attentional bias toward threat in anxious youth emerged relative to controls, but the difference was weaker than in adults. They also discovered that age was a significant moderator of attention bias: the magnitude of difference in attention biases between those

with and without anxiety increased with age. Thus, it may be that all children show attention biases for threat when they are younger, but as they mature into adolescence non-anxious youth lose or inhibit this bias, whereas anxious youth do not. However, moderator analyses found the between-group effect was only significant in the subgroup of studies using Stroop task, or in dot probe tasks at longer presentation times (1250ms). In contrast, a recent study by Abend et al (2018a) did find significant results with a 500ms dot probe task in this population. This study pooled data from multiple sites, totalling 1291 youth with varying levels of anxiety. Their results demonstrated attention bias toward threat at 500ms was positively correlated with anxiety symptom severity (however, there was no age moderation).

Taking these results together, RT tasks broadly suggest some level of attention bias toward threat in anxious youth but are relatively ambiguous as to whether this is more prominent in initial automatic attentional processing or at slightly later stages of attention where controlled/strategic processing may have more influence. Furthermore, whilst some RT tasks seem able to identify the presence of biased attention, others provide somewhat conflicting results. Understanding the nature of this bias more accurately may be hampered by the reliance on a single reaction time to measure a temporally-dynamic process. In light of this, recent studies have incorporated the use of eye-tracking methods, as a more direct measure of overt attention.

Results from studies employing measurement of first fixations to threat in anxious youth have also demonstrated contrasting findings; some studies have found anxious children and adolescents to have an initial orienting bias toward threat, relative to their non-anxious counterparts (Schmidtendorf, Wiedau, Asbrand, Tuschen-Caffier, & Heinrichs, 2018; Shechner et al., 2013), whilst others have found an association between anxiety severity and initial avoidance of threat (Kleberg et al., 2016; Price et al., 2016), others still have found no differences (Dodd et al., 2015; Heathcote, et al., 2016; In-Albon et al., 2010; Price et al., 2013). Only one study in the extent literature has used eye-tracking to investigate initial

maintenance, with Dodd et al (2015) finding no anxiety-related bias in initial maintenance of attention. In recording overall dwell time on threatening versus non-threatening stimuli (maintained attention) some studies have found a significant association between anxiety severity and overall avoidance (Michalska et al., 2017; Shechner et al., 2017), yet others have found no significant associations or group differences (Dodd et al., 2015; Price et al., 2016; Schmitendorf et al., 2018) - though Dodd et al (2015) did find a greater avoidance of all faces in anxious vs control children. Utilising time-windows, some results have demonstrated broad patterns of vigilance-avoidance in anxious young people (In-Albon et al., 2010; In-Albon & Schneider, 2012), though some have found no evidence of attentional avoidance with this method (Gamble & Rapee, 2009; Seefeldt, Krämer, Tuschen-Caffier, & Heinrichs, 2014). Therefore, eye-tracking studies have also provided somewhat varying results. However, variations in population and procedural variables, such as the relatively wide age differences between studies and differing stimulus array sizes, may have impacted these results to some extent.

Taking all attention bias findings together, evidence suggests attention bias appears to characterise anxious youth to some extent but may be expressed as biases both toward and away from threat, with multiple moderators likely affecting these findings. The only current meta-analysis in anxious youth does provide support for an overall attention bias toward threat, and a moderating effect of age. However, inconsistent findings within the research literature point to individual differences in the expression of this bias. It is likely some or all expressions of attention bias appear over the time-course of stimulus presentation – equating to a mix of (involuntary) bottom-up stimulus-driven mechanisms and (voluntary) top-down cognitive control mechanisms underlying the attention bias. It seems eye-tracking provides a promising method to gain some progress in our understanding of anxiety-linked attention biases, but extant literature using this approach in anxious young people also provides

differing results. However, with a relatively substantial number of eye-tracking studies now completed in this population, a meta-analytic review of these data is warranted.

1.4.2. Biases of Interpretation (and attribution)

As previously outlined, cognitive models suggest ‘schema-congruent’ biased interpretations of ambiguous cues are a maintaining factor in anxiety (Muris & Field, 2008). Ambiguous cues include stimuli that have both negative and benign meanings – with anxiety thought to be linked with more threatening/negative interpretations of ambiguous stimuli (Hirsch et al., 2016; Stuijzand et al., 2018). With it difficult to draw a firm distinction between threatening and negative interpretations, and as the same tasks have been used to measure anxiety and depression differences, much of the extant research has combined these categories into one general ‘negative valence’ category. There are now multiple adult studies showing a link between these ‘negative’ interpretations of ambiguous stimuli and anxiety (Hirsch et al., 2016): using several methods, research in adults has consistently found anxiety to be associated with both online (automatic) and offline (effortful) interpretation biases (Amir, Prouvost & Kuckertz, 2012; Hirsch & Mathews, 2000; Stopa & Clark, 2000; Voncken, Bögels & de Vries, 2003).

Tasks used to measure interpretation bias in children and adolescents

Interpretational style has been measured in anxiety using several methods. These methods can be utilised to measure both online and offline components of interpretational style. Online components can be defined as automatic inferences of ambiguous material, measured by tasks that prompt the individual for a response as soon as ambiguity is encountered in order to identify the interpretation that is immediately generated. In contrast, offline components refer to more effortful (or controlled) biases of interpretation, measured after the individual has had time to reflect on the ambiguous material.

The majority of studies have considered offline biases. To measure these biases one method makes use of ambiguous scenarios; in this ‘recognition task’ (Mathews & Mackintosh, 2000) the participants must complete the final word fragment to disambiguate a neutral sentence and later rate its similarity in meaning to a series of four similar sentences of varying valence. Originating as a measure for adult interpretations, this has been adapted to children and adolescents by using age appropriate scenarios. This task is used to measure effortful biases, in that it allows the participant time to reflect on the ambiguous stimuli before they are asked to provide an interpretation. Ambiguous situations are also utilised in the ‘sentence completion task’ (Huppert, Pasupuleti, Foa, & Mathews, 2007), which involves presenting the participant with a series of age-appropriate ambiguous sentences which they must complete with the first word that pops into their minds. These are then coded as threat or benign/positive in order to identify the bias. A similar approach comes in the form of the ambiguous situations questionnaire (Barrett, Rapee, Dadds, & Ryan, 1996). During this paradigm participants are presented with descriptions of hypothetical situations they may commonly encounter (e.g. “You see the head teacher walking around in the school yard, and hear they have been asking for you”) and are asked to give a free response to indicate what they think is happening in the situation (e.g. “Why do you think the headteacher wants to see you?”). This can also be followed with a forced choice selection of two options (threat/non-threat). Responses are then coded as threatening (e.g. “because I’m in trouble”) or non-threatening (e.g. “they have a message from my parents”). During some tasks participants also rate the given threatening and benign interpretations for likelihood. Recent studies have also employed methods to improve the ecological validity of interpretation bias measures by altering the ambiguous stimuli used; Haller, Raeder, Scerif, Kadosh, and Lau (2016) incorporated pictures of ambiguous social scenes into their ambiguous situations task to more closely mimic daily experience.

Online tasks used to measure interpretation biases often involve the use of ambiguous words; for instance, the individual may be presented with a series of homographs (words that are spelled the same but can have both a threatening and neutral/positive meaning, e.g. ‘hit’), and asked to create a sentence using the word. The sentence can then be coded as either threat or benign/positive. They can also be aurally presented with homophones (words that have the same pronunciation but different spelling and meaning, e.g. pain/pane) and asked to write the word down, which can then be coded as threat or benign/positive.

Evidence for interpretation biases in children and adolescents

There is fairly strong evidence to suggest that anxious youth endorse threatening interpretations of ambiguous events more often than non-anxious individuals, and benign/positive interpretations less often. Results from both clinical and non-clinical samples, using a range of these measures, suggest interpretation bias to be robustly associated anxiety: for instance, using an unselected sample of adolescents, Salemink and Wiers, (2011) found a positive association between threat-related interpretation bias and anxiety symptoms. Haller et al (2016) also recruited unselected adolescents and, with the use of their ambiguous visual scenes task, found unselected adolescents with higher levels of social anxiety rated negative interpretations as more likely (and positive as less likely) than those with lower social anxiety. A large recent study by Klein, de Voogd, Wiers, and Salemink (2017) tested almost 700 unselected adolescents (using the Interpretation Recognition Task; Mathews & Mackintosh, 2000) and found there to exist a significant correlation between interpretation bias and anxiety. Using a clinical sample, Bögels and Zigterman (2000) compared clinically anxious children and adolescents to clinical and non-clinical control groups and found greater negative interpretations of ambiguous situations in the anxious group compared to control groups. Studies of younger children have also found this interpretation bias to be evident (Barrett et al., 1996; Dineen & Hadwin, 2004; Hadwin et al 1997; Taghavi, Moradi, Neshat-

Doost, Yule, & Dalgleish, 2000). For instance, in a sample of unselected children using a pictorial homophone task, Hadwin et al (1997) found that interpretations of homophones were significantly predicted by anxiety levels. With a substantial amount of interpretation bias research now conducted in this population, a recent meta-analysis aggregated 345 effects sizes from 77 studies and found a medium positive association between anxiety and negative interpretation in children and adolescents (Stuijzand et al., 2018). Interestingly, this association was modified by age; the association increasing in strength as age increased. These results support findings by Waite, Codd, and Cresswell, (2015), who found that adolescents with anxiety disorders showed higher levels of threat interpretation than their non-anxious comparisons, but no difference in children under 10. These findings go hand in hand with previously discussed results of age moderating attention biases (Dudeney et al., 2015), and highlight age as an important factor in the emergence of anxiety-linked cognitive biases, as well as implying that treatment targeting these biases may have more impact in older children and adolescents.

Although research on attribution biases is highly limited, there is data to suggest socially anxious adolescents are more likely to internally attribute responsibility for negative events compared to positive events, such as task outcomes (Heimberg et al., 1989). Haller et al (2016) extended their investigation of interpretation bias to also measure how likely adolescents were to decide between internal or external causal attributions for social situation they had previously rated. The results showed that, compared to adolescents with lower levels of social anxiety, higher socially anxious adolescents were more likely to select internal attributions to negative social situations than to positive ones.

1.4.3 Summary

In summary, the research discussed demonstrates that cognitive biases of attention and interpretation do appear to underlie anxiety in adolescence, with age/development

moderating the effect of these biases. However, discrepancies in results of experimental studies in these areas also highlight some important features of current approaches that require development. RT measures of attention bias only provide only a snap-shot of attentional processes and are therefore limited in what they can tell us about the time-course and nature of attention bias; synthesis of results from eye-tracking studies of youth, may provide a more accurate index of attention bias. Interpretation bias studies show a more robust association with anxiety symptoms in children and adolescents, with age, and content specificity, moderating the strength of association between interpretation bias and anxiety. These cognitive biases may be amenable to change and provide accessible intervention targets. The next section discusses cognitive experimental tasks developed to modify the direction of the bias in order to assess causality, as well as evidence for their potential therapeutic effectiveness in anxious children and adolescents.

1.5. Modifying cognitive biases in children and adolescents: Overview of methods and findings

1.5.1 Modifying attention bias

Attention Bias Modification (ABM) training emerged first as an experimental manipulation method to alter attention-orienting patterns towards or away from threat or negative stimuli, and therefore assess whether biases in attention precede and cause symptoms (Eldar, Ricon, & Bar-Haim, 2008; MacLeod, Rutherford Campbell, Ebsworthy, & Holker, 2002). MacLeod et al (2002) first discovered that training adult participants to attend to negative stimuli showed a greater subsequent stress response than those trained away from negative stimuli. More recently, ABM methods have been implemented in randomised trials to investigate whether more adaptive attention-orienting patterns can be trained to reduce anxiety (Jones & Sharpe, 2017).

Tasks used to modify attention bias

The most common ABM method uses a modified version of the dot probe task in which the probe only ever appears in place of the non-threatening ('train-toward') stimuli (MacLeod, Mathews & Tata, 1986). Repeated practice of this process over many trials is proposed to result in habitual change in the existing automatic attention bias. Participants are most often trained away from threat using this procedure, due to the prevailing evidence of an anxiety-linked threat bias (Bar-Haim et al., 2007). If an ABM-Control condition is included in studies using this task, they will often use the same dot probe task, except with probes equally likely to replace threat and non-threat cues. A second ABM method is 'visual search' ABM training; as with the corresponding measure, the individual must select the non-threatening (target) stimulus amongst a host of threatening (distractor) stimuli as quickly as possible (Dandeneau & Baldwin, 2004). Again, repeating this process over many trials is designed to modify the existing bias. These tasks may differ somewhat in the processes they are targeting; While the dot probe task is designed to specifically train automatic threat-avoidant orienting, positive visual search training is may encourage disengagement and inhibitory control (Mogg & Bradley, 2016). If causally linked to anxiety, bias changes may lead to subsequent behavioural change.

Evidence for modification of attention bias in children and adolescents

Since early findings by MacLeod and colleagues (2002), there has been a substantial number of ABM studies in anxious and non-anxious individuals. The majority of studies have focused on adults, with some promising yet mixed findings; Meta-analyses have shown small to medium effects on attention bias and anxiety symptoms (Cristea et al., 2015a; Heeren et al., 2015; Linetzky 2015; Mogoşse et al., 2014), though a recent synthesis of CBM meta-analyses did find more promising results, finding ABM consistently modified targeted biases in adults (Jones & Sharpe, 2017). Eldar et al (2008) first investigated ABM with child participants, finding similar results to MacLeod and colleagues; since which there has been a

steady accrual of studies testing ABM approaches to improve anxiety in children and adolescents (Lowther & Newman, 2014). As per the adult literature, results from these studies have also be mixed; with some promising results, but also inconsistent reports regarding symptom change and successful modification.

The majority of studies in the younger populations have used the dot probe task initially implemented by MacLeod et al (2002). An early study by Bar-Haim, Morag, and Glickman (2011) found a significant improvement in response to a stress task following two session of ABM in high trait anxious children, as well as a change in attention bias, however no improvement in trait anxiety symptoms post-training. Several subsequent studies have also found promising, yet mixed, results with this approach; Eldar et al (2012) found significantly greater reductions in anxiety symptoms and severity in active ABM versus control/placebo groups after four ABM sessions. Riemann, Kuckertz, Rozenman, Weersing, and Amir (2013) found significant changes in self-reported symptoms across ABM and control groups, but a greater symptom reduction from ABM training (combined with CBT), though attention change was not measured. Rozenman, Weersing, and Amir (2011) also found significant improvement in symptoms after multiple ABM sessions, however no control group was employed for comparison and no significant change in attentional bias was found. Britton et al (2013), surprisingly, found an increase in bias toward threat after training children toward positive using a dot probe task; somewhat indicative of the inconsistency of findings in bias change across the field. Two subsequent studies testing dot probe ABM training for socially anxious adolescents have found no change in symptoms or attention bias compared to control groups (Fitzgerald, Rawdon, & Dooley, 2016; Ollendick et al., 2018). Thus, dot probe studies of anxious children and adolescents have provided early promise yet inconsistent findings subsequently, in terms of both symptom reduction and bias modification.

A number of recent studies have started to focus more readily on the visual search task as an alternative ABM tool, with five studies utilising this task in children and adolescents. Waters, Pittaway, Mogg, Bradley, and Pine (2013) found a greater reduction in attention bias and anxiety symptoms in anxious children who received twelve sessions of an “attention-towards-positive” visual-search training, compared to a control training condition. Using a novel positive visual search task, enhanced with learning and memory strategies, Waters et al (2015) again found that anxious children showed greater improvement in symptoms compared to waitlist controls. De Voogd, Wiers, Prins, and Salemink (2014) extended visual search training to the adolescent population and also reported greater reduction in social anxiety and attention bias change in adolescents who actively received two sessions of positive visual search training. These results provide promising findings for the use of the visual search task in anxious young people, yet recent studies testing the use of this task as an online ABM program have reported less consistent effects (de Voogd et al., 2016; de Voogd, Wiers & Salemink, 2017b), with some improvement found on attention bias, however no difference in symptom improvements between active and control/placebo group, suggesting bias change may have not been strong enough to evoke symptom change. These findings are perhaps unsurprising when taking into account the adult literature, which has also reported a lack of success with online ABM approaches (Boettcher, Berger, & Renneberg, 2012; Carlbring et al., 2012; Enock, Hofmann, & McNally, 2014). Furthermore, there are suggestions from qualitative results that ABM tasks are viewed relatively negatively by participants; reports suggest they see this training as boring and lacking any tangible goal (Beard, 2011; Brosan, Hoppitt, Shelfer, Sillence, & Mackintosh, 2011; de Voogd et al., 2016), possibly contributing to the inconsistent outcomes. Taken together, these results suggest ABM is less reliable outside controlled settings and, whilst the visual search task shows promise as an ABM tool, task improvements are necessary to more effectively and

consistently engage users before ABM tasks can be confidently utilised as a remote intervention tool.

Task engagement may be particularly pertinent for adolescents, some of whom display a preference for technology-based interventions over more traditional therapy (Spence, Donovan, March, Kenardy, & Hearn, 2017), but for whom online distractions are increasingly present (Moisala et al., 2016). In fact, a recent study by Abend et al (2018b) found that age has a significant impact on response to ABM, through its effects on learning. They conducted secondary analyses on two randomised control trials of ABM in adults and youth, with results suggesting younger participants find it more difficult to acquire the intended training contingency, which in turn may inhibit symptom reduction. Previous results support this assertion; Bar-Haim et al (2011) found that steeper learning curves within the ABM group were associated with lower anxiety in response to a subsequent stressor task.

Thus, development of attention training tasks that engage the participant and optimise their ease of learning appears a pressing objective within the field of ABM and a particularly pertinent target for improvement in the child and adolescent population. It may be that tailoring the task more effectively to the individual improves performance and outcome. Recent approaches have used real-time feedback of task performance, and gradual adjustment of task parameters, to individualise the task to the participant and optimise learning through re-enforcement (Bernstein & Zvielli, 2014; Schyner et al., 2015), with findings of successful attention bias change and symptom improvement. There is currently no research using individualised ABM-feedback tasks for anxious adolescents; however, based on these results, further research into this type of task adaptation could provide interesting results. Furthermore, individual differences in the nature of the existing attention bias prior to ABM may dictate the efficacy of ABM training in some individuals compared to others: in some adult studies attention bias at baseline has been shown to affect the magnitude of change in both attention bias and anxiety symptoms from ABM training (Amir, Taylor, & Donohue,

2011; Fox, Zougkou, Ashwin, & Cahill, 2015). Although some child and adolescent studies have looked for associations between initial threat bias and symptom change (Waters et al., 2015), there are no studies at present evaluating how initial bias direction may influence efficacy of ABM training. Understanding how characteristics of attention bias at baseline affects ABM outcome may provide further clues as to how tasks can be best individualised for optimal results.

Taken together, ABM studies in child and adolescent anxiety have provide mixed evidence for the causal impact of attention bias on anxiety symptoms. Substantial variation in ABM delivery make assessing causality very difficult. The visual search task appears a promising ABM tool, however (much like the dot probe task) improvements in training efficacy are required to overcome weak or inconsistent effects. Thus, a key question for future research centres on how the effects of ABM can be enhanced in anxious youth.

1.5.2 Modifying interpretation bias

Much like ABM methods, Cognitive Bias Modification for Interpretations (CBM-I) first emerged as a method for testing the causal link between interpretation biases and mood (Mathews & Mackintosh, 2000). It has since been developed and implemented in randomised trials to investigate whether more adaptive interpretative style can be trained to improve anxiety and depression.

Tasks used to modify interpretation bias

The most widely used CBM-I method is the ‘ambiguous situations task’ (Grey & Mathews 2000; Mathews & Mackintosh, 2000). During this task participants are presented with a series of ambiguous sentences and a final incomplete word fragment. Completion of the final word resolves the sentence and disambiguates the valence in a positive direction. Participants then receive a follow-up ‘yes/no’ question with ‘correct/incorrect’ feedback in

order to reinforce the training. The aim being that, through repeated trials and practice, this will encourage more adaptive styles of interpretation processing. Although this was initially developed for adults, this method has been adapted for use with children and adolescents by retaining the basic task parameters but modifying the stimuli content and modality. The administration format varies between studies, with most recent studies presenting information on computer screens, where earlier studies used printed cards.

Evidence for modification of interpretation bias in children and adolescents

Accumulation of results using CBM-I in anxious adults has led to multiple meta-analyses, showing positive effects of CBM-I on interpretation bias but slightly more mixed findings on symptom reduction (Cristea, Kok, & Cuijpers, 2015b; Hallion & Ruscio, 2011; Menne-Lothmann et al., 2014). Almost all CBM-I studies in anxious children and adolescents have utilised the ambiguous situations task, with some relatively promising findings for bias change and anxiety reduction. In a meta-analysis combining all CBM approaches in young people, Cristea and colleagues (2015b) found a moderate effect of CBM training on interpretation bias, but no significant overall effects on anxiety. However, a more recent meta-analysis by Krebs et al (2017), identified 27 studies using CBM-I alone in individuals from clinical and community samples, aged between 6 and 18 years. The authors found that CBM-I had a statistically significant moderate effect on both decreasing negative interpretations and boosting positive interpretations, as well as a small but significant effect on self-reported anxiety immediately following training. The results suggest interpretation bias can be modified in both healthy and anxious adolescents, however, resultant changes in anxiety are less readily achieved.

As with ABM research, meta-analyses for CBM-I are also hindered by the heterogeneous approach to training tasks, session numbers and measures; with some moderators identified yet difficult to disentangle in adults (Menne-Lothmann et al., 2014).

CBM-I delivery in the extant literature varies considerably, possibly explaining this effect – however, it should also be noted that many of the existing studies have been single session, with only a handful of multi-session studies existing. In fact, Krebs and colleagues (2017) only identified eight of their included studies to have used multiple sessions. Whilst mood may be altered by simple repeated exposure to the stimuli in single sessions, significant changes in trait anxiety may require multiple sessions of training, possibly evoking a stronger change in interpretation style (Lau, 2013; Menne-Lothman et al., 2014). Adult meta-analyses have seen a trend for greater anxiety effects from multi-session CBM-I than from single session approaches (Hallion & Ruscio, 2011); thus, more multi-sessions studies in youth are required to investigate possible differences in efficacy from multiple training sessions. Furthermore, the vast majority of research in the adolescent population has been conducted using community samples of healthy participants. Of the twenty-seven studies included in Krebs et al meta-analysis, only seven were conducted amongst either clinically anxious participants or those with elevated anxiety symptoms. Therefore, whilst results are promising in terms of modifiability of interpretational style in youth samples, there needs to be more research in this population with individuals experiencing elevated anxiety and the use of multi-session approaches. Additionally, there appears to be a lack of research investigating symptom reduction effects with ecologically valid measures of anxiety, which may show stronger effects. For instance, a study by Lau, Belli, and Chopra (2013) found more consistent training effects when adolescents were presented with psychological challenge induced in the laboratory post-training. Only seven studies included in the meta-analysis by Krebs et al (2017) used a measure of anxiety post-stressor. Further research using more ecologically valid tests of emotional regulation, such as real-life stressful situations, is required in order to more accurately capture these changes.

Much like ABM investigations, inconsistent results mean greater task engagement and receptivity is becoming a key focus of CBM-I approaches. Some studies have started to

investigate the type of stimuli presentation used to provide a more engaging experience for the individual, with the aim of more effectively accessing the biased cognitive processes. Menne-Lothman et al., (2014) discovered greater mood effects when imagery was used in CBM-I. Indeed, research has shown that processing information via imagery evokes greater emotional responses (Holmes & Matthews, 2010) and stronger increases in positive mood and bias modification (Holmes, Mathews, Dalgleish, & Mackintosh, 2006) compared to verbal processing. However, one recent attempt to incorporate imagery into an online version of CBM-I for adolescents with elevated anxiety symptoms provided no improvement over word-based and placebo comparison groups, suggesting further enhancement of imagery-based CBM-I approaches are necessary (de Voogd et al., 2017a). Individualising the tasks further to the specific disorder being addressed appears to be one potential direction - The recent meta-analysis by Stuijzand et al (2018) found that, when measuring cognitive biases in anxious youth, the content of ambiguous scenarios presented to participants moderated the relationship between anxiety and interpretation bias; with stronger associations when the scenarios matched the anxiety disorder (largely driven by socially anxious individuals). This suggests disorder specific imagery may boost the effectiveness of CBM-I when addressing specific disorders such as social anxiety.

Targeting appraisal more directly

Cognitive reappraisal is employed as an emotion regulation strategy subsequent to initial appraisal of stimulus, where the individual attempts to change their initial interpretation of the affective stimuli and thus regulate the emotion evoked (Schäfer, Naumann, Holmes, Tuschen-Caffier, & Samson, 2017). Identification of neural networks correlated with adaptive emotion regulation (ER) strategies, such as reappraisal, provide another interesting opportunity to boost cognitive training approaches (Hare et al, 2008; Ochner & Gross, 2005) by extending individualisation to the brain level. One strategy is to employ ‘mechanism-

driven' cognitive training; i.e. attempt to change the neural substrates of emotion regulation and feed this information back to the individual as a type of reinforcement learning (Linden et al., 2012). 'Neurofeedback (NF)' gives explicit real-time information regarding the individual's brain activity in emotion areas during the rehearsal of emotion regulation strategies; thus, providing a tangible learning reference to increase development of effective strategies. Furthermore, in personalising the task to the individual by providing feedback of their performance, this is more likely engage them in the task. Preliminary results from neurofeedback training in adolescents show that the use of these techniques to improve learning of emotion regulation strategies and reduce levels of anxiety is promising (Kadosh et al., 2016). However, there is currently no evidence as to whether this effect transfers to improved emotion regulation outside the scanner. It's possible that the use of this technology to improve adaptive emotion regulation training (such as cognitive reappraisal) may enhance its effectiveness and improve subsequent emotional reactivity to perceived threat.

Taken together, the evidence presented in the preceding paragraphs suggests CBM-I has potential to impact upon anxiety symptoms in young people, however further research is required to understand whether improvement of several areas of delivery is able to enhance the weak effects on anxiety symptoms reported in a recent meta-analysis (Krebs et al., 2017). Modality of stimulus presentation, content specificity, and multiple sessions are all areas for further investigation and could further boost modification effects. Furthermore, individualisation of tasks, possibly drawing upon cognitive neuroscience approaches, may further boost adaptive strategies in reappraising perceived threat, potentially leading to improved symptom reduction.

1.4.4. Combined cognitive biases

A final reflection on the modification of cognitive bias, is that the majority of studies have investigated cognitive biases in isolation, however it is possible there may be interplay

among these processes that may have important contributions toward symptom maintenance (Everaert, Koster, & Derakshan, 2012; Hirsch, Clark & Mathews, 2006). If individual cognitive biases only play a limited role in anxiety, targeting these biases in isolation may be restrictive in producing the strongest possible effect, thus targeting these biases in combination may produce a greater magnitude of change (Hirsch, Clark & Mathews, 2006). Only one study has previously utilised a combined-bias approach to CBM training in anxious adolescents: an RCT (Sportel, de Hullu, de Jong, & Nauta, 2013), with two-year follow up (de Hullu, Sportel, Nauta, & de Jong, 2017) tested an online combined CBM-I/CBM-A program and found no significant difference between internet-based CBM (designed to target attention and interpretation biases), CBT, and control group; with all groups showing significant improvement in symptoms at six-month and two-year follow-up. Further research is needed to follow up on these preliminary findings.

1.4.5 Summary

In summary, results from CBM-I and ABM studies have shown some promise in modifying cognitive biases and reducing trait anxiety, yet results have been inconsistent. ABM studies have not consistently managed to modify attention biases or reduce symptoms - the number of sessions, frequency of training and number of trials clearly varied between the studies, perhaps contributing to the differential changes in attention bias, and make assessing causality very difficult. Recent studies using online-ABM have not found symptom reduction effects, and qualitative studies suggest task engagement is poor for existing methods, suggesting new modification methods must be developed to consistently change existing attention biases. CBM-I utilising a single session of training compared to multiple sessions has shown less successful bias modification, and much like ABM, recent studies using internet- or remote-based CBM-I have largely failed to find symptom reduction effects. This indicates that, much like the attention bias literature, further research is required to

understand the task parameters required to most effectively modify interpretative style and reduce symptoms of anxiety in young people. The calculation of real-time task performance to provide (implicit/explicit) feedback to the individual throughout the task could provide greater learning optimisation and task engagement in CBM approaches. Finally, targeting these cognitive biases in combination may improve modification outcome.

1.5. Thesis aims and study questions

The research presented throughout this chapter provides an illustration of the severity and high prevalence of anxiety in young people. Adolescence appears to be a period of significant onset for anxiety disorders and may also provide an optimal intervention period. The evidence suggests that cognitive biases of attention and interpretation do appear to underlie anxiety in youth, with age/development potentially moderating the effect of these biases. However, reaction time measures of attention bias have provided especially inconsistent results. Eye-tracking presents an option to more directly measure attentional deployment and may provide a clearer picture of attention bias expression underlying anxiety in youth.

It appears these cognitive biases can be modified, with some impact on subsequent anxiety, indicating causality of some magnitude. However, evidence from CBM approaches is currently inconsistent and/or weak in magnitude, meaning efforts to improve these approaches are crucial. The discrepancies in results of experimental studies in these areas highlight some important features of current approaches that require development. There is a lack of multi-session CBM studies, targeting multiple cognitive biases in combination; single-session/single-bias approaches may not be enough to prompt symptom change in some individuals. Furthermore, improving task individualisation and engagement may boost training outcomes. Incorporation of real-time feedback of behavioural and neurobiological indices of performance provides a promising approach to improve task engagement and

learning optimisation in cognitive training.

Therefore, this thesis will focus on evaluation of cognitive training methods to enhance the modification of anxiety-linked cognitive biases in adolescents, and assessment of the expression of attention bias in anxious youth. Outlined below are the four empirical chapters that aim to investigate the issues presented above, broadly arising from the themes of *attention* and *appraisal (interpretation/attribution/reappraisal)*:

Chapter two addresses whether we can use eye-tracking to obtain a clearer picture of the expression of *attention bias* in youth anxiety. Meta-analyses of extant data are carried out by compiling effect sizes from studies using eye-tracking in anxious youth to investigate threat vigilance and maintenance. **Chapter three** spans both of the above themes by addressing whether CBM is boosted by targeting biases in combination; this chapter investigates the effectiveness of an enhanced CBM programme for adolescents with elevated social anxiety. Specifically, investigating whether targeting cognitive biases in combination, over multiple sessions with disorder-specific task stimuli, can improve social anxiety symptoms in adolescents.

The second half of the thesis builds upon results from the *chapter three* by evaluating the use of real-time feedback to boost effectiveness in modifying *attention* and *reappraisal*.

Chapter four aims to boost modification of *attention*, with the development and evaluation of a new real-time feedback method of ABM focused on improving task engagement and learning optimisation to achieve stronger bias modification effects than standard ABM training. **Chapter five** investigates whether we can utilise developments from cognitive neuroscience to individualise cognitive training at the brain level and more directly boost adaptive emotion regulation, in the form of positive *re-appraisal*. This is carried out by evaluating the use of neurofeedback training in adolescents, with the aim of improving subsequent reappraisal ability and anxiety-related avoidant behaviour. Finally, **chapter six**

summarises all findings from these investigations and provides interpretations of results in synthesis with extant literature followed by suggestions for future directions.

Chapter 2

2

Eye-tracking of attention to threat in child and adolescent anxiety: a meta-analytic study

Attention biases for threat may reflect an early risk marker for anxiety disorders, yet questions remain on the nature and time-course of these biased attention patterns in children and adolescents. This chapter presents the first meta-analysis of eye-tracking studies of biased attention for threat in anxious children and adolescents, assessing the presence of vigilance towards threat and maintained attention on threat, and any between-group differences with non-anxious youth. A systematic literature search was conducted using anxiety, children and adolescent, and eye-tracking-related key terms. After screening for eligibility, 13 studies involving 798 participants were included. A random effects model was used to estimate between- and within-group effects of first fixations toward threat and between-group effects of overall dwell time on threat. Publication bias was assessed. Neither children/adolescents with or without anxiety showed significant bias in first fixation (vigilance bias) to threat versus neutral stimuli, and there was no difference between groups. Children and adolescents with anxiety showed significantly less overall dwell time on threat versus neutral stimuli (avoidance bias), compared to non-anxious controls ($g = -0.26$). In contrast to adult data, and data from reaction time indices of attention biases to threat in children and adolescents, there appears no absolute bias in initial fixation to threat in anxious youth or any differences to non-anxious youth. However, over the entire time-course of stimulus viewing anxious children and adolescents are more avoidant of threat than their non-anxious counterparts.

2.1 Introduction

Effective detection of danger is a normative function that is fundamental to survival. However, some individuals can be hypersensitive in their attentional processing of threat-related information, contributing to an interruption of healthy daily functioning. Threat-related attentional bias refers specifically to biases in selective attention toward and away from threat-related information and has been implicated in maintenance of anxiety disorders (Bar-Haim et al., 2007; Dudeney et al., 2015). Over the past several decades experimental tasks relying on Reaction Time (RT) have been used to probe the presence of attention biases and their links with anxiety disorders. Meta-analytic reviews combining data for RT measures of attention biases in adults (Bar-Haim, 2007), and children and adolescents (Dudeney, 2015), have broadly found a more exaggerated early (automatic) bias towards threat in anxious versus non-anxious individuals. However, results between individual studies have provided inconsistent findings regarding the presence and direction of this bias, as well as the expression of maintained attention over longer viewing periods where strategic processes have a greater influence. This may, in part, be due to RT measures only providing an indirect measure of attention via a manual key press and relying upon a single score as an index of attention bias at the end of stimulus viewing. Eye-tracking (ET) measures, that directly measure the location and duration of gaze fixations throughout stimulus presentation, and thus give a more direct and continuous measure of overt attention, may provide a more accurate indication of initial vigilance to threat, and favoured location of maintained attention over the entire viewing period. Meta-analyses of adult eye-tracking studies have shown similar pooled results to RT meta-analyses (Armstrong & Olatunji, 2012) - a greater initial vigilance toward threat in anxious versus non-anxious individuals. These eye-tracking methods have now been utilised in a substantial number of research studies to measure attention biases in children and adolescents. At present, there is no single quantitative review pooling this data together; therefore, the objective of the present meta-analysis is to assess ET

results when investigating initial vigilance to threat in anxious children and adolescents, and evaluate ET results of maintained attention across time, as an extension of existing RT results. The chapter will begin with a brief outline of attention bias research in anxiety. Following this we will present meta-analyses of findings from eye-tracking studies that investigate initial vigilance to threat and maintained attention, in child and adolescent anxiety.

2.1.1. Theoretical considerations of attention bias

Information-processing models of anxiety propose an attention bias to threatening information (Bar Haim, 2007; Cisler & Koster, 2010; Mogg & Bradley, 2016; Muris & Field, 2008; Williams et al., 1988), yet the expression of this bias is debated (Cisler & Koster, 2010). Differing theoretical accounts have proposed the contribution of several components of anxiety-linked attentional bias: some propose facilitated *threat-orienting (vigilance hypothesis)*, in which automatic attention is captured more readily or more quickly by threatening stimuli amongst anxious individuals (Bar-Haim, et al., 2007; Beck & Clark, 1997; Eysenck et al., 2007); others propose *attentional maintenance on threat*, putting forward that it is maintained attention on threat that characterises anxiety, in which anxious individuals demonstrate *difficulty disengaging* from threat following attentional capture (Fox et al., 2001, 2002); furthermore, some suggest *avoidance of threat*, a prominent aspect of the vigilance-avoidance hypothesis (Mogg et al., 2004) in which it is suggested strategic attentional avoidance of threat follows initial vigilance towards threat. Importantly, these components may all play a role; it is possible that initial vigilance may be followed by difficulty disengaging from threat, and subsequent strategic avoidance of threatening stimuli across the time-course of stimulus viewing (Weierich et al., 2008).

2.1.2. Reaction time (RT) measures of attention

Research from RT measures of attention have provided varying levels of support for anxiety-linked attention bias. The majority of attention bias research to date (Bar-Haim et al., 2007; Dudeney et al., 2015), has relied on RT-based measures such as the Stroop task and the dot probe task (as outlined in chapter 1), in which attention bias to threat is inferred from differences in RT to threatening and non-threatening stimuli. The dot probe task is a measure of visual spatial orienting – i.e. it gives an indication as to the location of the individual's attention when the probe appears, allowing us to infer in which direction there lies an attentional bias; short presentation times ($\leq 500\text{ms}$) are used to measure vigilance, whereas longer display times (around 1250ms) are designed to measure the location of maintained attention. The Stroop task does not measure spatial orienting, but instead allows for measurement of the individuals' ability to inhibit the processing of distracting emotional information, however, attentional processes underlying any effect cannot be separated; therefore, most recent investigations have utilised the dot probe task.

The use of these tasks in child and adolescent anxiety has amassed a relatively substantial amount of data yet yielded mixed results: dot probe tasks have found varying results of attention bias toward and away from threat at both automatic and strategic stages of processing, as well as findings of no bias. Dudeney and colleagues (2015) pooled together findings from thirty-eight of these studies and found anxious and control groups both displayed a significant attention bias toward - in contrast to adult meta-analyses which found a within-group threat-bias for anxious but not non-anxious adults (Bar-Haim et al., 2007). However, consistent with adult meta-analyses, they also discovered anxious youth demonstrated a greater bias toward threat than non-anxious youth. Furthermore, the strength of this difference increased with age from childhood to adolescence. However, they also found effects to be stronger for studies using the emotional Stroop tasks than the dot probe task; which only demonstrated a between-group difference in bias toward threat in studies

using 1250ms presentation time rather than shorter presentation times (500ms or less). This raises questions as to how strongly anxiety-linked attention bias in youth is driven by vigilance for threat, and the comparative influence of stimulus-driven (bottom-up) attention and later strategic (top-down) processes. In fact, these moderator results are in direct contrast to adult findings; Bar-Haim et al (2007) found studies employing dot probe tasks with up to 500ms exposures demonstrated significant differences between anxious and control participants, whereas longer exposures failed to reach significance. Dudeney and colleagues speculate as to whether fatigue and errors in response accuracy may be more pronounced in children and adolescents, or perhaps a longer time is needed to process stimuli before the button press.

Therefore, combining effect sizes from RT studies leaves ambiguity as to the expression of attention bias in anxious youth; i.e. is there an initial vigilance toward threat during automatic processing or does an attention bias occur during more strategic attentional deployment? Indeed, these results also demonstrate the limitations of RT measures in how accurately they can index attention bias; as they only provide a measure of attention through a manual keypress at the end of stimulus viewing, before which multiple processes may have occurred.

2.1.3. Limitations of RT-based measures

Due to the distal relation between behavioural response and attentional processing, RTs can only provide a relatively indirect measurement of attention, often described as a “snapshot” of attention in the moment of response (Armstrong & Olatunji, 2012). This makes identification and measurement of specific components proposed to underpin attention bias (such as facilitated threat orienting) more difficult to achieve, particularly within a single trial. Whilst RT tasks are able to separate individual components, they require multiple conditions in order to achieve this (e.g. altering stimulus presentation times to investigate

initial vigilance vs subsequent avoidance of threat or using a spatial cueing task to isolate threat disengagement, (Fox et al., 2001)). Furthermore, the dot probe was not designed to examine extended eye-gaze patterns; with attentional deployment likely to vary significantly in the longer time period prior to probe appearance, the resultant RT score is unable to account for the variation in attentional processing before probe appearance. Additionally, confounding factors such as preparation and execution of motor response may vary between individuals and therefore affect results from RT tasks (Armstrong & Olatunji, 2012). Therefore, whilst RT measures provide important insights into the link between attention and anxiety, developments in the field have seen the incorporation of alternative approaches to complement RT methods, in an attempt to more directly measure attention across the viewing period.

2.1.4. Eye-tracking as a more direct measure of attention

Eye-tracking has been proposed as a route to more directly monitor attention across time. This method comprises several measures of eye data, including saccades (the quick movements of eyes across the stimuli; Salvucci & Goldberg, 2000) fixations (time and location of attentional deployment between saccadic movements; Salvucci & Goldberg, 2000), and pupillometry (an index of physiological response by measurement of change in pupil size; Keil et al., 2018). Continuous recording of this data allows for analysis of attentional deployment throughout the time-course of stimulus presentation (Duchowski, 2007). This has obvious advantages over RT measures when investigating attention biases: recording of these eye movements and fixations provides a closer and more direct measurement of attention than that of a manual button press. For instance, we can monitor the exact location of the first fixation, to give a very specific measure of initial orienting, and thus an indication of which type of stimulus the individual is vigilant towards. Furthermore, as this approach allows for the continuous recording of gaze throughout display time, we can

gain a more accurate picture of which stimulus is more likely to maintain attention throughout the trial.

Attentional deployment may be conceptualised as ‘covert’ or ‘overt’: covert attention refers to the deployment of attention without shifting of gaze, whereas overt attention involves the orienting of attention via eye movement. As such, eye-tracking methods are only able to measure overt attention. Whilst this can be seen as a limitation of the method, research suggests that overt eye movements mediate the effects of (and are directed by) covert attention (Armstrong and Olatunji, 2012; Hayhoe & Ballard, 2005; Kowler et al., 1995). Importantly, as pointed out by Armstrong & Olatunji (2012), this attentional relationship is much closer than that of covert attention than manual responses (e.g. a button press). However, it should be noted that covert attention does not necessarily always lead to overt eye-movements (Hunt & Kingstone, 2003).

2.1.5. Eye-tracking approaches to measure attention bias in anxiety

In order to use this method to obtain an index of attention bias, it is combined with attentional viewing tasks. The most prevalent task used in ET studies of child and adolescent anxiety is the free-viewing design (Garner, Mogg, & Bradley, 2006). During this passive-viewing task the individual is presented with two or more stimuli of contrasting valence (e.g. threat and neutral) on the screen and instructed to view the presented stimuli in any way they wish whilst their gaze is tracked. One advantage of this method in child and adolescent populations is the ability to obtain meaningful and reliable data during passive viewing; whereas in younger children, with less developed motor functioning, the reliance on a button press as an index of attention has resulted in reports of poor task reliability (Brown et al, 2014).

Whereas RT tasks require multiple conditions to separate specific aspects of attention, the use of ET, combined with viewing tasks, allows for observation of multiple aspects

within a single trial (Armstrong & Olatunji, 2012), including vigilance to threat, and maintained attention, but also disengagement of initial attention (initial maintenance), and vigilance/avoidance patterns across time. Whilst the latter two components are beyond the scope of this meta-analysis (due to studies available), we nevertheless provide an overview of measures used in eye-tracking research of attention bias, for the sake of clarity:

Vigilance. Vigilance toward threat can be measured by recording the location of the individual's *first fixation* after stimulus presentation, in each trial. Comparison of first fixations to threat against first fixations to neutral provides a probability score to indicate the direction of initial orienting. Greater probability of first fixation toward threat indicates the presence of a threat vigilance bias. An alternative approach is to compare the latency of first fixations to each stimulus type – this is the time until first fixation is executed. Faster first fixations to threatening versus neutral stimuli are also proposed to indicate a vigilance bias.

Initial maintenance. In order to measure initial maintenance on threat, as an index of difficulty disengaging from threatening stimuli, the *duration of each first fixation* is recorded. Mean duration of first fixation to threat compared to that of non-threatening stimuli, provides an indication of initial maintenance/disengagement. Greater duration on threatening than non-threatening stimuli suggests delayed initial attentional disengagement from threat.

Maintained attention. In order to measure maintained (or sustained) attention on threat across stimulus presentation time, *overall dwell time* on each stimulus type is calculated, across the entire trial. Therefore, this measure provides an indication of attentional behaviour to threat that has already been detected. Greater mean dwell

time on threatening stimuli than on non-threatening stimuli provides an indication of maintained attention toward threat. The opposite would suggest an overall avoidance of threat.

Attentional avoidance. A more detailed measure of attentional avoidance patterns over the time course of stimulus presentation utilises *time-windows*, or epochs. Dwell time on threatening and non-threatening stimuli are calculated per window (e.g. every 500ms) in order to determine patterns of attention allocation across time. Specifically, observations of reduced dwell time on threat during the time-windows following automatic attentional deployment allow for identification of subsequent strategic avoidance.

2.1.6. Eye-tracking results from studies in anxious adults

A substantial amount of studies of anxious adults have made use of this technology to probe anxiety-linked components of attention. A recent meta-analysis by Armstrong and Olatunji (2012) pooled together effect sizes from studies using these approaches in order to evaluate differences in initial vigilance and initial maintenance biases. They discovered that during free viewing and visual search tasks anxious adults demonstrated greater initial vigilance for threat compared to non-anxious adults. However, they did not investigate total dwell time on threat versus non-threat stimuli over the entire stimulus presentation time. Therefore, their findings provide strong support for results showing vigilance for threat during initial orienting in adults (Bar-Haim et al., 2007), however no conclusions regarding overall direction of maintained attention.

2.1.7. Eye-tracking in anxious children and adolescents

Developmental differences in attention networks means we are unable to extrapolate adult findings to child and adolescent populations, and therefore, of particular importance in understanding anxiety onset and development, is the employment of these methodological advancements in studies of young people. This allows for investigation of how attention biases in adults may differ in their relation to anxiety amongst younger participants (when onset of anxiety often occurs; Kessler et al., 2007), and how consistent they are with previous RT findings in the child and adolescent populations. Eye-tracking measures have been steadily employed in younger samples of anxious and non-anxious participants, with the majority of studies investigating vigilance to threat, by measuring probability of first fixation towards threat, and maintained attention on threat, by measuring total dwell time on threatening/non-threatening stimuli. Therefore, with a relatively substantial amount of research now available for investigations of vigilance and overall maintained attention in this population, it is appropriate to pool the extant eye-tracking data to evaluate combined effect sizes on these measures. Consequently, the overall aim of this study is to provide a systematic assessment of the relationship between attention bias and anxiety in children and adolescents using eye-tracking methods. Specifically, we aim to investigate whether a threat vigilance bias exists, using probability of first fixation to threat, and whether an attentional bias toward or away from threat is present in maintained attention, i.e. total dwell time on threat.

2.1.8. Procedural and Population-related moderators

Inconsistent findings across studies investigating anxiety-related attentional biases, involving RT and eye-tracking approaches, in both young people and adults, may be due to various methodological inconsistencies that remain valid for the studies included in this meta-analysis. As researchers alter task parameters (e.g. presentation time, passive vs active viewing) and investigate specific sub-populations (e.g. 16-18 yr. olds with clinical social

anxiety only) in order to address their specific research goals, it is important to recognise that there are significant procedural and population variations within this literature, which will need to be taken into account as possible moderating factors during analysis. Therefore, the following moderators were selected a priori:

Sample Age. Empirical evidence suggests attention bias may vary with age (Dudeney et al., 2015). Theoretical accounts have suggested that all children may begin with an attention bias toward threat when then “corrects” during healthy developmental trajectories (Field & Lester, 2010). In turn, this suggests findings from studies using specific age ranges (e.g. child / adolescent) may capture a unique attentional response to threat, which may not necessarily translate to other ages.

Attention task. Attention tasks in this population vary between a strictly free-viewing approach and dot probe task - which contains a free-viewing element and a subsequent active component of probe selection. The probe identification element in the dot probe task may result in anticipatory eye-movements during the free-viewing element, thus affecting first fixation results – Studies have shown the presence of anticipatory saccades prior to stimulus presentation in eye-movement studies (Rommelse et al., 2008).

Presentation time. Presentation time may also moderate findings. With relatively short presentation times believed to capture automatic attentional deployment and longer viewing times believed to capture more strategic processes (Mogg & Bradley, 2014), analyses of total dwell-time from studies using markedly different viewing times may be prone to differential influences of automatic and strategic processes. Armstrong and Olatunji (2012) suggest that attention bias beyond around 2000ms may fall into the category of

strategic, whereas before that time there may be a greater combined influence of automatic and strategic processes.

Anxiety group. Findings may be moderated by the clinical features of the sample (Pergamin-Hight et al., 2015). A large proportion of research studies investigating attention biases use samples containing individuals with mixed anxiety diagnoses or features, however this may moderate the intensity of the threat stimuli used in the tasks. For instance, socially salient threat stimuli (such as the emotional faces often used in attention bias tasks) may provoke more exaggerated responses in socially anxious individuals than those with other anxiety types, (Chen et al., 2002; Dudeney et al., 2015; Pergamin-Hight et al., 2015; Waters, et al., 2014).

Clinical diagnosis. Finally, some studies have found a threat-bias only occurs amongst high clinically anxious youth, with lower anxious individuals sometimes found to display no bias or a bias in the opposite direction (Waters et al., 2010; 2011). Therefore, it may be the case that symptom severity modifies the expression of the attention bias. Theoretical accounts suggest that those with higher levels of anxiety severity lack the strategic cognitive control to allow them to regulate attentional capture by threat and thus display a more pronounced bias (Waters et al., 2011). Therefore, incorporating this moderating factor into the meta-analysis will be important in probing the effect of anxiety severity on attention bias expression.

2.1.9. Aims and Objectives

With the aforementioned factors in mind, the aim of this meta-analysis was to evaluate attention bias to threat in anxious children and adolescents, by combining effect sizes of studies using eye tracking methodology. Specifically, we aim to address the

following questions: firstly, do anxious children/adolescents and their non-anxious counterparts show an absolute bias (significantly different from zero) in probability of first fixation to threatening stimuli (as an index of initial threat-vigilance)? Secondly, is there a between-group difference on this vigilance measure? Thirdly, do anxious children/adolescents and their non-anxious counterparts show an absolute bias in total dwell time on threat versus neutral stimuli (as an index of maintained attention)? Fourth, is there a between-group difference in total dwell time on threat versus neutral stimuli? Finally, do population and procedural factors moderate these results?

2.2. Methods

2.2.1. Inclusion Criteria

The criteria which all studies were required to meet to be eligible for inclusion in the meta-analysis were:

1. The study must be available in English.
2. The study must be an original investigation, not a review paper.
3. The study must investigate a sample of human participants ≤ 18 years of age.
4. The study must use a standardised measure of anxiety (state or trait) for all participants; either clinical interview or a self/parent-report anxiety questionnaire.
5. The study must use eye-tracking to measure attention biases.
6. The study must use a free-viewing task, or task with a free-viewing element (such as dot probe), during which attention is tracked.
7. Appropriate data must be available to allow for the computation of an effect size for at least one of the bias measures being investigated (probability of first fixation to threat; latency of first fixation to threat; total dwell time on threat versus neutral). This

may be available as mean scores for ‘anxious’ and ‘non-anxious’ groups, a test statistic for group difference, or a correlation between the attention measure and anxiety severity. If these data are unavailable in the paper, they must be made available by the author.

8. The design must allow for the comparison of attention towards threatening and neutral elements of the array. Studies pairing threatening stimuli with stimuli of any other valence were excluded (e.g. Lagattuta and Kramer (2017), who paired fear and angry faces with a mixture of happy and neutral faces).

2.2.2. Literature Search and Study Selection

The literature search was conducted in April 2018. Pubmed, Psycharticles, Medline, Psycinfo and Embase databases were searched for eligible studies. We used anxiety related key terms; anx*, anxiety disorder, GAD, depress*, fear, phobi*, dysphori*, and panic. These were crossed with key terms to eye-tracking measures; eye*, gaze*, fixation*, dwell time, and saccade. We also crossed these with key terms to identify children and adolescent participants; (child*, adol*, pediatric, youth, juvenile, and teen*. Reference lists of identified studies were also used to identify further potentially eligible research, as were relevant review papers. All searches were made from database start until April 2018. Titles and abstracts were screened for inclusion by the authors and a fellow graduate student based on criteria 1-5. Studies that met this eligibility criterion were retained for full-text review to assess whether they met all criteria. Subsequently, all retained articles were reviewed in full by the author and two further colleagues to assess whether they met the full set of inclusion criteria. Reference lists of the studies meeting all inclusion criteria were checked for further eligible studies. Where studies met all inclusion criteria, but further data was required, authors were contacted to request the necessary data.

2.2.3. Data coding system and coding decisions

Studies were coded on the following variables: a) number of participants, b) participants' mean age, c) Gender split (% female), d) sample type (clinical/analogue), e) type of anxiety disorder, f) experimental task (free-viewing / dot probe / other), g) type of threat stimulus (face / picture), h) threat emotion, i) number of stimuli presented, j) stimulus presentation time. When the study included results from 'with/without stressor' groups separately, data from the without stressor condition was used in order to retain consistency across the sample (k=2).

2.2.4. Meta-analytic method

Definition of Vigilance and Maintenance

Meta-analyses were carried out to test two aspects of attention bias. Firstly, the vigilance hypothesis was examined – that individuals with an anxiety disorder will detect threat more readily, and thus orient to it more often, than non-anxious controls. Secondly, we tested the maintenance hypothesis – that anxiety is characterised by maintained attention to threat; thus, across the entire trial, individuals with anxiety will more often dwell upon threatening than neutral stimuli. The vigilance hypothesis was investigated using studies that recorded the direction of initial gaze orienting; specifically, measures of probability of first fixation to threat vs neutral stimuli and latency of first fixation toward threatening stimuli were used. Studies that did not report first fixation probability or latency, but only reported total fixation time on threatening stimuli in the first 500+ms, were excluded from the analysis (k=2). The maintenance hypothesis was investigated using studies that recorded the mean duration of gaze (dwell-time) toward threat versus neutral stimuli, when stimuli was displayed for longer than 1000ms.

With these measures, we aimed to perform within-group analyses of attention bias in first fixation toward threat for anxious and non-anxious groups, in order to evaluate any presence of an ‘absolute’ bias toward threat in either group. We also sought to understand the between-group difference between anxious and non-anxious individuals on this measure. Due to a lack of relevant data for within-group analysis of attentional maintenance, only between-group analysis could be carried out for this attention bias measure.

Effect size calculation

All effect sizes were calculated using Hedges’ g . To interpret effects with this measure, Cohen’s d (1988) guidelines can be used; small effect = .20, moderate effect = .50, large effect = .80. For the between-group analysis of both vigilance and maintenance, effect size direction was calculated so that a positive effect size indicates the attentional bias toward threat is larger in anxious participants than in control participants. In studies that did not use high and low symptom groups, correlations between symptom severity and attention bias were used, with a positive effect size indicating a greater attention bias toward threat for more anxious individuals. In the within-group analyses, a positive effect size indicates that the attentional bias is greater for threat stimuli than neutral stimuli, with a negative effect size indicating the opposite. Meta-analyses were conducted using comprehensive meta-analysis software (version 3.3.070). A random-effects model was chosen to compute combined effect sizes, as heterogeneity was expected across studies, and this method allows the results to be generalized to similar studies (Field, 2001). To assess heterogeneity of overall effect sizes, Cochran’s Q (Hedges & Olkin, 1985) was used. Additionally, the I^2 statistic (Higgins & Thompson, 2002) was used, indicating the percentage of this variation across effect sizes that is down to heterogeneity rather than chance.

Categorical variables were identified as potential moderators, consisting of population and procedural factors that differed across studies. Population variables included: Age group

– Adolescent (mean age of 12 years and above) or Child (mean age below 12 years); Sample Type – Clinical or Analogue; Anxiety Type - SAD/SP (Social Anxiety Disorder / Social Phobia) or Mixed (more than one anxiety disorder included). Procedural variables included: Attention task – Dot probe or Free-viewing; Stimulus presentation time – 2000ms and below or Greater than 2000ms. Due to the number of samples available, there was insufficient power to investigate the influence of moderators, such as age and presentation time, through meta-regressions (as would usually be preferable for variables such as these); therefore, subgroup analysis was used for all moderator variables. Moderator analyses were conducted in relation to outcomes on between-group measures of vigilance and maintenance. Due to the small number of studies eligible for within-group analysis moderator analysis was not carried out for the within-group results.

Risk of publication bias

Funnel plots were inspected for all analyses to assess publication bias (see appendix A). Rank correlation (Begg & Mazumdar, 1994) and regression tests (Egger et al., 1997) were also carried out to evaluate evidence of publication bias, as well as Duval and Tweedie's trim and fill method (Duval & Tweedie, 2000). Fail-safe numbers were computed to assess the magnitude of a potential file-draw problem – this provides an estimate of the number of studies, with an effect size of zero, that would need to be added to the analysis to produce a cumulative effect that is statistically non-significant ($p > .05$). In addition to this, we used Orwin's (1983) fail-safe N to calculate the number of studies with an effect size of zero that would need to be added to the analysis to produce a specified “trivial” Hedges' g value.

2.3. Results

2.3.1. Search Results

Figure 2.1. illustrates the literature search and study selection process. Initial searches identified 3871 studies. After removing duplicates, this was reduced to 1818 studies. After excluding by abstract, this number was reduced to 29 studies. Full-text screening resulted in the exclusion of a further 16 studies, resulting in 13 eligible studies.

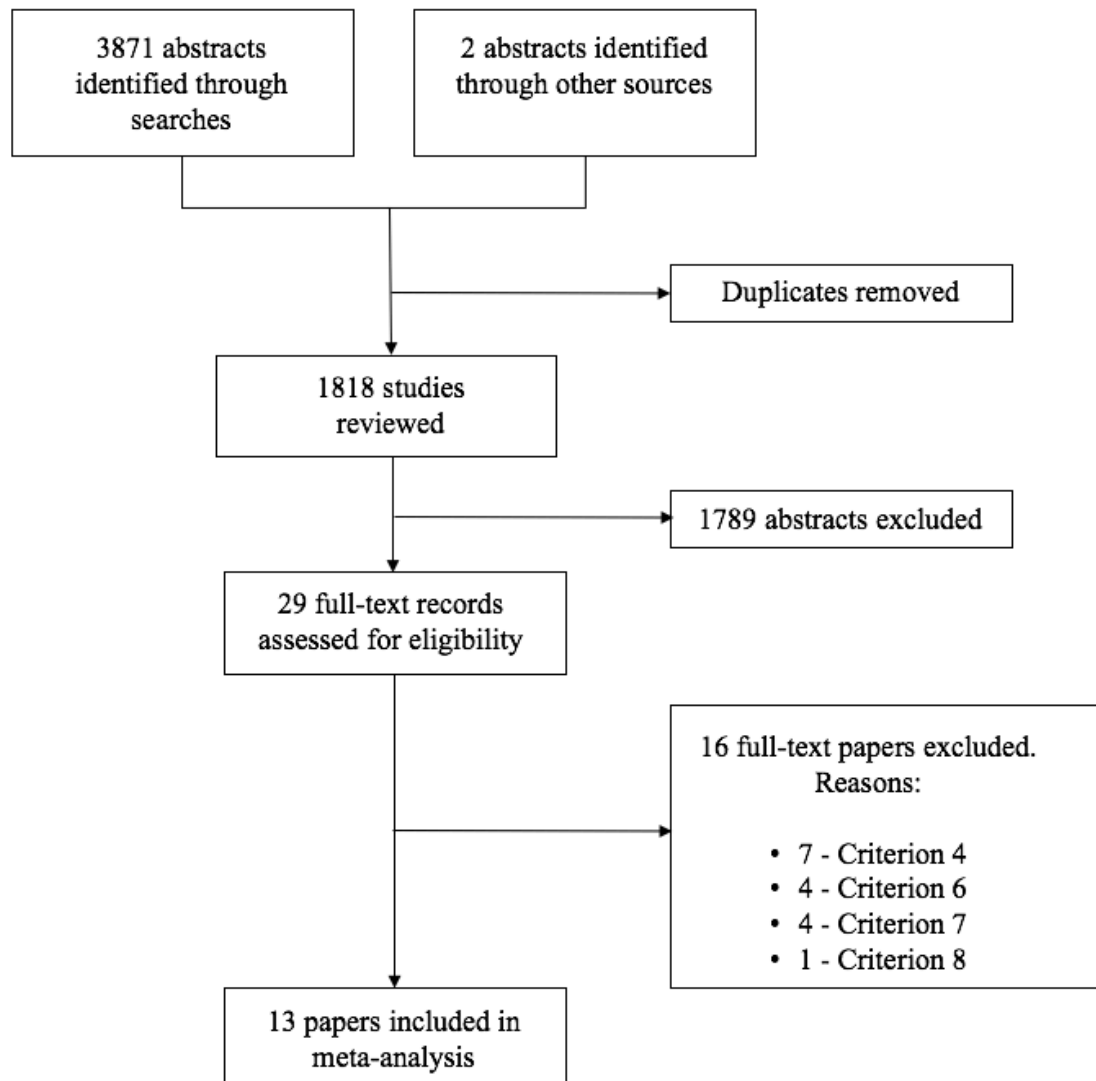


Figure 2.1. Flowchart of screening processes for study inclusion. Criterion 4: did not use standardised measure of anxiety; criterion 6: did not use appropriate attention task; criterion 7: necessary data was unavailable/unobtainable; criterion 8: did not allow for comparison of attention towards threatening and neutral stimuli.

2.3.2. Study Characteristics

Study characteristics are displayed in Table 2.1. The entire data set was scanned for outliers; these were identified as studies whose 95% confidence intervals did not overlap the 95% confidence interval of the combined effect size. No studies yielded an effect size that was an outlier. Therefore, the total sample included data from 798 participants aged 3-18 years, from 13 studies. All studies were published in peer-reviewed journals. All studies used an attention task containing a free-viewing element, though the specific tasks varied across studies; 9 studies used a task that solely involved free-viewing of the presented stimuli, whereas 4 studies used a dot probe task that required a user action after the period of free-viewing. Of the 13 studies, 9 used a clinical sample of anxious participants, and 4 used an unselected sample. Of the 13 studies, 5 investigated attention bias in relation to social anxiety disorder (SAD) or social phobia (SP), 2 used broader overall anxiety scores, 1 for state anxiety, and the remaining 5 included patients with a mixture of anxiety diagnoses (including SAD, SP, generalised anxiety disorder (GAD), and separation anxiety (SEP)). Most studies (10) used faces as the threatening stimuli – 5 of these using an angry emotion, 3 using fear, 1 using pain, and 1 specifying a general “threatening” face was used. 2 studies used eyes as the threatening stimuli – one as part of the face, and the other using a picture only of the eyes. The final 1 study used pictures of social scenes – with various faces in social scenes defined as the threatening stimuli. Effect sizes within each study, and confidence intervals, can be seen in Figures 2.2. to 2.4.

Table 2.1 Study Characteristics

Study	N	n (clinical)	n (control)	Age Range	Mean age (years)	% female	Sample type	Primary anxiety problem	Attention task	Threat stimulus	Threat emotion	Number of stimuli	Display Time (ms)
Capriola-Hall et al. (2018)	41	41	N/A	Adolescents (12-16)	14.54	68%	Clinical	SAD	Free-viewing	Face	Angry	2	3000
Dodd et al. (2015)	83	37	46	Children (3-4)	3.99	59%	Clinical	SAD, GAD, SEP, SP	Free-viewing	Face	Angry	2	1250
Haller et al. (2017)	51	N/A	N/A	Adolescents (14-18)	16.73	100%	Analogue	SAD	Free-viewing	Scene	Social	Varying	5000
Heathcote et al. (2016)	37	N/A	N/A	Adolescents (8-17)	12.1	64%	Analogue	State anxiety	Free-viewing	Face	Pain	2	3500
Kleberg et al. (2017)	25	25	N/A	- Adolescents	15.2	84%	Clinical	SAD	Free-viewing	Eyes	Eyes	4	2000
Michalska et al. (2017)	82	N/A	N/A	Children (9-13)	11.81	60 %	Analogue	Overall anxiety score	Free-viewing	Face	Eyes	1	7000- 8000
Price et al. (2013)	94	74	20	Children -	10.57	52%	Clinical	GAD, SEP, SP	Dot probe	Face	Fear	2	2000

Price et al. (2016)	67	67	N/A	Children (9-14)	11.1	53.7%	Clinical	GAD, SEP, SP	Dot probe	Face	Fear	2	2000
Schmidtendorf et al. (2018)	79	37	42	Children -	11.45	61%	Clinical	SAD	Free-viewing	Face	Angry	2	5000
Seefeldt et al. (2014)	73	30	43	Children (8-12)	9.9	44%	Clinical	SP	Dot probe	Face	Angry	2	3000
Shechner et al. (2013)	33	18	15	Adolescents (8-17)	13.19	58%	Clinical	GAD, SAD, SP	Free-viewing	Face	Angry	2	10000
Shechner et al. (2017)	45	19	26	Adolescents (8-17)	12.63	44%	Clinical	GAD, SAD, SP	Free-viewing	Face	Threat	3	5000
Tsypes et al. (2017)	88	N/A	N/A	Children -	9.26	44%	Analogue	Overall anxiety score	Dot probe	Face	Fear	2	1000

Note: GAD = generalized anxiety disorder; SAD = social anxiety disorder; SP = social phobia (spider); SEP = separation anxiety disorder.

2.3.3. Meta-analysis of anxiety and vigilance

Within-group Analyses

The meta-analyses examining within-group differences in vigilance toward threat versus neutral stimuli (fig. 2.2), show that the combined effect size was not significant in anxious participants ($k=6$; $g=0.315$, $p=.21$, $CI= -0.17, 0.80$), or in non-anxious controls ($k=6$; $g=0.27$, $p=.27$, $CI= -0.21, 0.75$). There was large heterogeneity in the effect sizes for anxious ($Q(5) = 46.32$, $p < .001$, $I^2=89.20\%$) and non-anxious ($Q(5) = 39.48$, $p < .001$, $I^2=87.33\%$) groups.

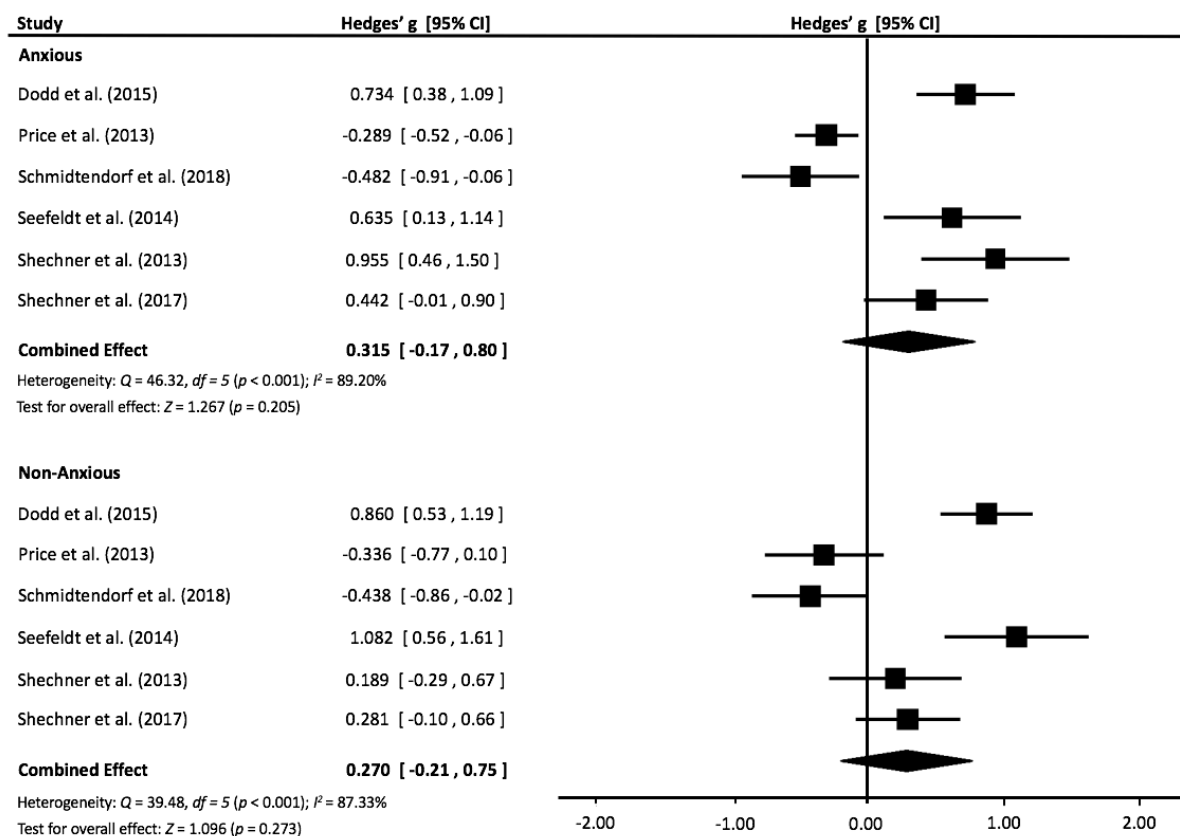


Figure 2.2. Forest plot of within-group initial orienting bias for threatening stimuli, with 95% confidence intervals and study weights illustrating contribution to overall effect size. Diamond represents estimate of combined effect size.

Between-group Analysis

The meta-analysis examining the between-group differences in vigilance to threat (fig. 2.3) found that anxious individuals did not significantly differ from non-anxious individuals in initial orientation of attention towards threatening versus neutral stimuli ($k=8$; $g=0.04$, $p=.39$, $CI=-0.18, 0.26$). There was not significant heterogeneity in the effect sizes, $Q(8) = 8.56$, $p = .29$, $I^2=18.25\%$.

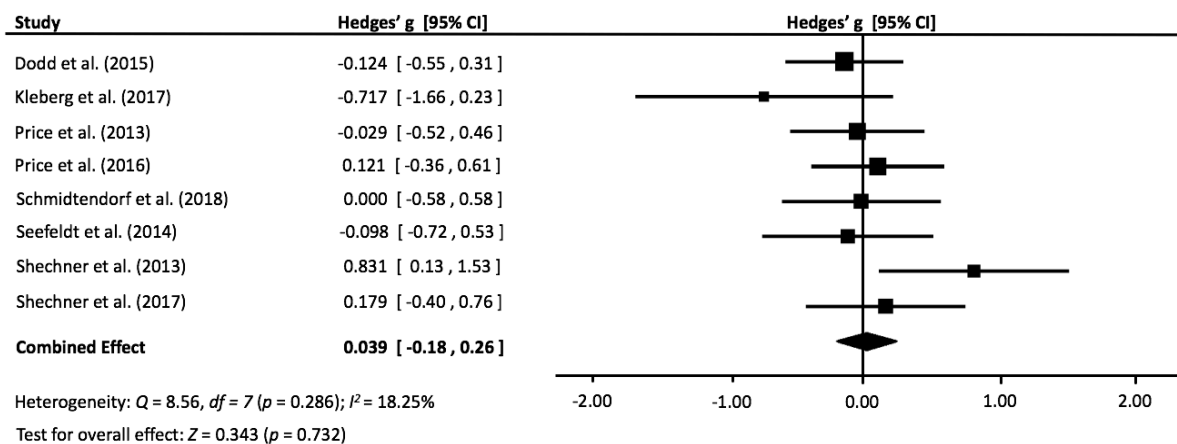


Figure 2.3. Forest plot of between-group initial orienting bias for threatening stimuli, with 95% confidence intervals and study weights illustrating contribution to overall effect size. Diamond represents estimate of combined effect size.

2.3.4. Meta-analysis of anxiety and maintained attention

Between-group Analysis

The overall effect size for the meta-analysis examining the association between anxiety and maintenance (fig. 2.4) was significant ($k=12$; $g = -0.26$, $p=.004$, $CI=-0.44, -0.08$), indicating anxious individuals were more inclined to avoid threatening stimuli than non-anxious individuals during maintained attention. There was not significant heterogeneity in the effect sizes, $Q(11) = 15.48$, $p = .162$, $I^2=28.93\%$.

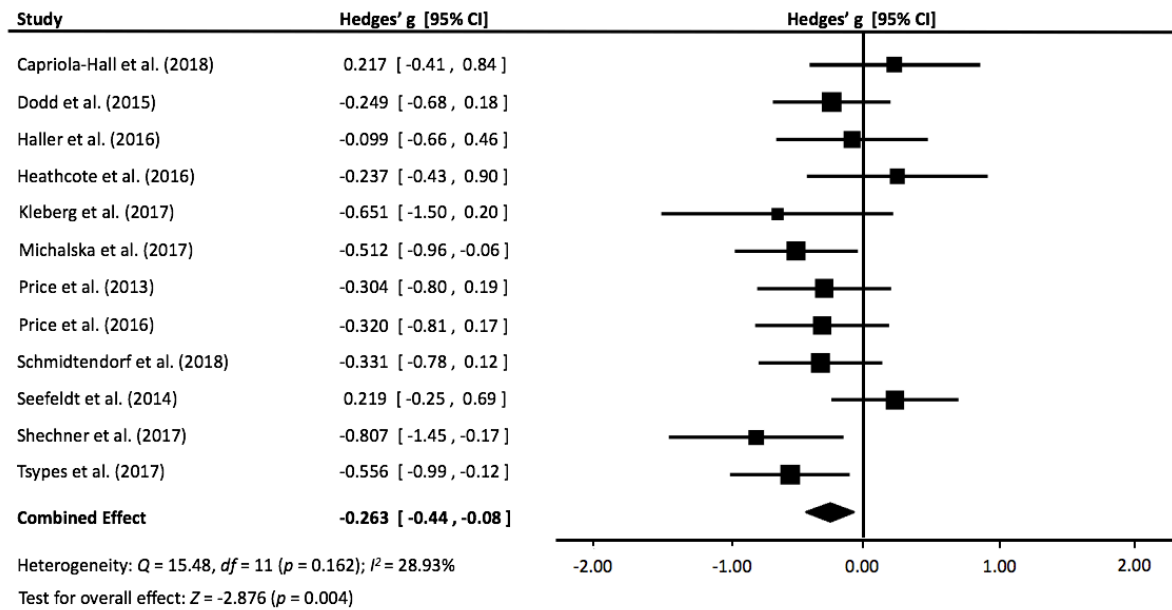


Figure 2.4. Forest plot of maintenance bias for threatening stimuli, with 95% confidence intervals and study weights illustrating contribution to overall effect size. Diamond represents estimate of combined effect size.

2.3.5. Sub-group moderator analyses

The non-significant χ^2 values in testing for heterogeneity in variance, and I^2 values that aren't extremely high, suggests the studies in each sample were fairly homogenous. However, as the I^2 values were approaching 25%, and based upon a priori analysis plans, moderator analyses were conducted. Furthermore, χ^2 tests have been shown to only have adequate power if there is a large difference between population effect sizes, or there is a moderate difference but the number of effect sizes is large (Cortina, 2003; Sackett, & Orr, 1986), yet excessive power to detect negligible variability when a large number of effect sizes are included (Cornwell, 1993; Cornwell & Ladd, 1993; Medina, Sanchez-Meca, Marin-Martinez, & Botella, 2006).

Sub-group moderator results for between-group comparisons of attentional vigilance

There were no significant moderation effects on attentional vigilance by population or procedural factors identified a priori.

Table 2.2. Moderator results for between-group comparisons of attentional vigilance

	<i>Effect size</i>			<i>Heterogeneity</i>	<i>Moderation</i>	
Moderator	k	g	95% CI	I²	Q	p
Age group						
Adolescent	3.00	0.15	-0.62, 0.93	70.27	0.20	0.66
Child	5.00	-0.03	-0.25, 0.2	0.00		
Presentation Time						
<2001ms	4.00	-0.07	-0.33, 0.19	0.00	1.36	0.24
>2000ms	4.00	0.20	-0.18, 0.58	32.90		
Task						
Dot probe	4.00	0.01	-0.26, 0.28	0.00	0.06	0.81
Free-viewing	4.00	0.08	-0.44, 0.6	63.17		
Anxiety Type						
Mixed	4.00	0.21	-0.11, 0.54	26.71	2.61	0.11
SAD/SP	4.00	-0.14	-0.43, 0.15	0.00		

Note: SAD = Social Anxiety Disorder; SP = Social Phobia; Mixed = studies including patients with a range of anxiety diagnoses. The number of studies using an analogue group (k=0), was not enough to test moderation of “sample type”. Significant effects ($p<.05$) denoted by *.

Sub-group moderator results for between-group comparisons of attentional maintenance

For anxiety type, significantly greater (negative) between-group effect sizes (indicating more *avoidance* of threat for anxious compared to non-anxious individuals) was found for studies including participants with a mixture of anxiety types, than for studies using only social anxiety ($p=0.050$).

Table 2.3. Moderators results for between-group comparisons of attentional maintenance

Moderator	<i>Effect size</i>			<i>Heterogeneity</i>	<i>Moderation</i>	
	k	g	95% CI	I²	Q	p
Age group						
Adolescent	5	-0.19	-0.61, 0.22	49.82	0.20	0.653
Child	7	-0.30*	-0.48, -0.11	14.22		
Presentation Time						
<2001ms	5	-0.35*	-0.60, -0.16	0	1.37	0.242
>2000ms	7	-0.16	-0.45, 0.13	50.47		
Task						
Dot probe	4	-0.24	-0.57, 0.09	49.04	0.02	0.881
Free-viewing	8	-0.27*	-0.5, -0.05	26.70		
Sample Type						
Analogue	4	-0.30	-0.63, 0.04	41.35	0.07	0.791
Clinical	8	-0.24*	-0.46, -0.02	29.77		
Anxiety Type						
Mixed	6	-0.43*	-0.63, -0.24	0	3.83*	0.050
SAD/SP	5	-0.08	-0.37, 0.21	14.07		

Note: SAD = Social Anxiety Disorder; SP = Social Phobia; Mixed = studies including patients with a range of anxiety diagnoses. Significant effects ($p < .05$) denoted by *.

2.3.6. Publication bias

Funnel plots were inspected, and no evidence of asymmetry was observed. Egger's test (Egger et al., 1997) and rank correlation tests (Begg & Mazumdar, 1994) were all non-significant (all $ps > .49$). Furthermore, using the Duval–Tweedie trim and fill procedure (Duval & Tweedie, 2000), no evidence of publication bias was found for any of the measures. For the maintenance meta-analysis, the fail-safe N (Rosenthal, 1979) was 37, meaning there would need to be 25 studies with an effect size of zero added to the analysis to increase the p -value to above .05, i.e. produce a statistically nonsignificant cumulative effect.

In addition to this, using Orwin's fail-safe N, in order to bring our criterion down to a Hedges g value of $-.1$, it would take 21 extra studies with an effect size of zero.

2.4. Discussion

2.4.1. Summary of findings

This chapter provides the first meta-analysis of eye-tracking measures of attention bias in child and adolescent anxiety. Data was included from 13 studies, totalling 798 participants, between ages 3 and 18 years. The first aim of this study was to determine whether first fixation of attention was biased toward threatening stimuli for anxious and/or non-anxious participants. Anxious individuals did not show a significantly greater tendency to direct first fixations on threatening over neutral stimuli, and neither did non-anxious individuals. The second aim was to evaluate whether there was a difference in first fixation bias between anxious and non-anxious participants. No between-group difference emerged. Thirdly, we aimed to understand whether anxious and non-anxious participants differed in their overall allocation of attention across the trial. The results indicated that anxious individuals showed a greater tendency to avoid maintaining their gaze on threat compared to non-anxious individuals. Finally, we aimed to understand which conditions moderated the emergence of attention bias differences between anxious and non-anxious youth; there was a significant moderating effect of anxiety type on maintained attention.

2.4.2. Initial vigilance toward threat

In a review of adult ET studies, Armstrong and Olatunji (2012) found a greater tendency to first fixate on threat in anxious than non-anxious individuals. In contrast, we find no such difference. The results from this meta-analysis suggest biased orienting toward threat doesn't differentiate anxious and non-anxious youth; and are therefore not consistent with the

vigilance hypothesis suggesting anxiety is characterised by facilitated detection and orienting of initial attention toward threat. However, these findings are not incompatible with child and adolescent RT results; the meta-analysis of RT studies by Dudeney et al (2015) found no evidence of a between-group difference for studies measuring spatial orienting with a dot probe task at 500ms, but only with studies using the Stroop task; a measure more sensitive to measuring inhibition of distracting stimuli than spatial orienting (Reinholdt-Dunne, Mogg, Esborn, & Bradley, 2012). When they did see a difference in spatial orienting it was found with studies using the dot probe after 1250ms presentation time, which is likely to be measuring attentional deployment beyond initial fixation. We also found no within-group vigilance effect in anxious or non-anxious children and adolescents, and no moderating effect of age on between-group differences in vigilance. These data therefore seem to speak against developmental accounts that all children begin with an attention bias toward negative faces which then “corrects” during healthy developmental trajectories (Dudeney et al., 2015; Field & Lester, 2010; Kindt et al., 2003), and suggests there may be other developmental pathways to maladaptive attention allocation (Waters & Craske, 2016). However, caution is needed before drawing any firm conclusions. Firstly, we do see significant heterogeneity of variance for both anxious and non-anxious groups in the within-group analyses, however we did not have enough studies to look at moderator influence for these meta-analyses. Therefore, a vigilance bias for threat may yet be apparent when measuring vigilance in only pre-adolescent individuals. Secondly, in conducting moderator analysis on the between-group vigilance findings, the relatively small number of samples prevented adequate power to investigate the influence of age through a meta-regression. Instead we relied on sub-group analysis, which crudely used mean age of the sample to dichotomously categorise studies into children and adolescents. This approach, along with the fact that many studies used wide age ranges, means these moderator results should be interpreted with caution. Furthermore, it should be noted that whilst these first fixation results do suggest no attentional bias in initial

orienting toward threat, they don't provide any indication regarding initial maintenance on threat, which may still differ between anxious and non-anxious youth (and/or be biased amongst all **children, as per the developmental** literature) following the first fixation.

In fact, whilst the measure of initial orienting via eye-tracking does provide a more precise measure of eye movement, and thus provides a valuable indication of where overt attention is first directed, it can be questioned whether the first fixation measures reflect purely exogenous (stimulus driven) attention or whether this indicates a mixture of stimulus-driven and strategic processes. Previous research has found a typical latency of exogenous first fixations to be around 175ms (Rayner, 1998), whereas ET studies from anxious individuals have generally shown first fixation latency to be longer (around 250ms - 400ms; Garner et al., 2006; Mogg et al., 2000), thus suggesting the representation of initial vigilance we can take from eye-movements (EMs) in anxious individuals likely contains some endogenous influence, and probably doesn't capture purely stimulus-driven attention that RT tasks with very short presentation times might. There are also suggestions first fixation measures aren't as reliable as one would hope (Lazarov, Abend, & Bar-Haim, 2016; Waechter, Nelson, Wright, Hyatt, & Oakman, 2014; Wermes, Lincoln, & Helbig-Lang, 2017). Waechter et al (2014) found poor reliability for first fixation measures of attention bias, suggested to be due to significant "look-up" and "look-left" biases, indicating results may be affected by participants favouring fixation to the top or left image regardless of its emotional valence. They did find a high reliability for 'proportion of total dwell time' across the entire viewing period (5000ms), but when dividing this period up found the first 1500ms to show low reliability.

The free-viewing approach employed by many eye-tracking studies may also impact upon identifying anxiety group differences in first fixations. As this task only measures spontaneous viewing behaviour, and not attentional behaviour related to task demands, it may be less powerful in its ability to tap into attentional engagement/disengagement as neither are

necessary for task completion. Research has indicated group differences in attention bias are more readily identified when a task action is required, such as visual search task (Huijding et al., 2011; Rinck et al., 2005), especially when searching for an emotion-irrelevant feature of the display (Dodd, Vogt, Turkileri, & Notebaert, 2017).

Therefore, these results testing the vigilance hypothesis indicate there is no significant difference in overt initial orienting between anxious and non-anxious youth, however results must be interpreted with caution regarding reliability, and regarding generalisation of this measure to purely stimulus-driven attentional response or beyond this component of attentional deployment.

2.4.3. Maintained attention

The meta-analysis of maintained attention found that, averaged over the course of viewing, anxious individuals showed a greater tendency to avoid maintaining their gaze on threat compared to non-anxious individuals. Thus, it appears across longer levels of stimulus viewing, where top-down voluntary control processes are more influential, there is an avoidance of threatening stimuli amongst anxious (relative to non-anxious) youth. This is in contrast to our hypothesis that the anxious group would be characterised by maintained attention upon threatening stimuli. This overall attentional avoidance is somewhat in contrast to adult ET studies that have often found greater maintained attention on threat in anxious individuals when using mean dwell-time measures (Buckner, Maner, & Schmidt, 2010; Lazarov et al., 2016; Liang, Tsai, & Hsu, 2017; Schofield, Johnson, Inhoff, & Coles, 2012; Wieser, Pauli, Weyers, Alpers, & Mühlberger, 2009).

However, location of maintained attention may also be specific to the type of anxiety disorder. In fact, the only factor that appeared to significantly moderate maintained attention was ‘anxiety type’; studies using only social anxiety as the primary anxiety category/measure were unable to observe the between-group effect, whereas studies using participants with a

mixture of anxiety types did. It should be noted that studies using mixed anxiety groups all included social anxiety patients within their samples; plus, with a relatively high level of homotypic comorbidity in anxiety disorders (Beesdo et al., 2009), several of the social anxiety studies may also have included other comorbid anxiety disorders, making it difficult to disentangle biases in maintained attention per disorder. However, as a whole, the results do imply that specific diagnostic sub-groups other than SAD are driving this avoidance effect. In fact, utilising more specific disorder and symptom boundaries in study designs may provide more insightful results in future as attentional components are increasingly being found to show disorder and symptom specificity (Grafton, Southworth, Watkins, & MacLeod, 2016; Southworth, 2015). Research has shown specific subsets of symptoms to be associated specifically with just one expression of attentional bias; for instance, Grafton et al (2016) found rumination of negative thoughts to be associated specifically with difficulty disengaging from negative stimuli. Indeed, even within disorders, differences have been found regarding attentional deployment based upon symptom severity; one RT study found that children with more severe social anxiety displayed a bias towards threat, whereas those with mild (yet still diagnosed) social anxiety exhibited a bias away from threat, (Waters, Mogg, Bradley, & Pine, 2011).

One salient point arising from this measure of attention is that it may not be always be accurately identifying biases in maintained attention / avoidance of threat due to differences in threat evaluations— for instance, research has found that all facial stimuli may be considered somewhat threatening in socially anxious individuals due to their indication of potential social evaluation, and as such avoidance of all faces may occur (Kuckertz, Strege, & Amir, 2016; Mansell, Clark, Ehlers, & Yi-Ping Chen, 1999). In fact, avoidance of all perceived social threat, such as direct eye-gaze (Roelofs et al., 2010), may mask any attention bias picked up with current measures, as only between-face differences are generally calculated. Only one study included in this meta-analysis measured avoidance of faces

overall (Dodd et al., 2015) and found that the anxious group were more avoidant of all faces than the non-anxious group, yet no between-face difference emerged. As most studies included in this meta-analysis used just two stimuli, avoidance to other areas of the screen may be more likely than in studies using a larger array of faces.

In fact, more naturalistic social scenes with multiple competing stimuli may help improve upon this and other issues: research has shown that gaze capture by threatening stimuli is affected by the number of other competing stimuli present and how closely clustered the stimuli are (Calvo, Nummenmaa, & Hyönä, 2008; Yates, Ashwin, & Fox, 2010). Furthermore, arrays of small stimulus set sizes may lack the ecological validity provided by larger arrays of stimuli (Richards et al., 2014) – larger displays of competing stimuli may increase the similarity to every-day situations and thus produce a more natural response. Indeed, results may well be context dependent; for instance, Chen, Clarke, MacLeod, Hickie, and Guastella (2016) found that when gaze was tracked in socially evaluative situations (such as having to give a speech) there was an attentional avoidance of threat; however, in studies of free-viewing emotional pictures findings have indicated sustained attention towards threat (Lazarov et al., 2016). Only one study in the meta-analysis used a visual social scene (Haller et al., 2016) – more studies employing complex scenes with multiple competing stimuli (and gaze measures incorporating the whole display) may allow for a more ecologically valid measure of attentional deployment.

The mean dwell-time bias score is also unable to infer specific patterns of attention over time, where biases toward and away from threat may both separate anxious and non-anxious individuals at various time-points. Thus, whilst this measure gives us an idea of the “overall” direction of attentional deployment, specific patterns of attention this overall direction is comprised of cannot be readily identified with this measure. Furthermore, as the total dwell time score also includes initial deployment of attention, it is not possible to conclude our results indicate “subsequent avoidance following initial orienting”, but rather

just a mean preferential effect. Studies utilising time-windows, or dwell-time from second fixation onwards, are better placed to investigate this; there are studies available in child and adolescent anxiety that investigate the pattern of attention across the viewing period using time-windows (Gamble, & Rapee, 2009; In-Albon et al., 2010; In-Albon & Schneider, 2012), however several were unable to be included in the meta-analysis as they did not satisfy the inclusion criteria and/or the relevant data was unavailable. Further research utilising time-windows with consistent parameters, enabling comparison across studies, would help elucidate possible patterns of attention thorough meta-analyses.

The moderating effect of age was of particular interest due the proposed impact of development on attention bias expression (Field & Lester, 2010). Whilst not reaching significance as a moderator, when categorising the studies by age the child category showed a significant avoidance whereas the adolescent studies did not. Tentatively, one could suggest this indicates an attentional avoidance of threat that may be stronger in younger people, but changes with age through to adulthood. This is surprising, as the literature proposes avoidance is a maladaptive emotion regulation strategy, largely driven by executive control processes developed through youth (Amso & Scerif, 2015; Paus, 2005). However, as discussed above, it should be noted that multiple studies included participants with a relatively wide age range that crossed the child/adolescent boundary but did not consider the moderating effect of age within the study. Therefore, we were only able to use mean age to dichotomously categorise these samples containing relatively wide age ranges. Furthermore, as per the vigilance analysis, due to the relatively small number of samples, we were unable to investigate the influence of age through a meta-regression. Therefore, age can only be seen as a broad proxy for development in this case. Additionally, there was a relatively high heterogeneity of variance between effect sizes in the adolescent group, indicating other factors may be affecting these results. Further research focused on the association between

anxiety-linked attention biases and specific developmental factors would help elucidate the development of attention bias in anxious youth.

Several other moderators also found differential effects that may have reached significance with larger samples. Studies employing display times of 2000ms or less showed significant overall avoidance, whereas those using longer times did not. This may indicate rapid avoidance strategies following initial fixations that dominate the earlier period of stimulus viewing; however, the relatively high I^2 value for the '>2000ms' category also suggests this finding was impacted by other factors. Likewise, the 'clinical' category reached significance whereas the 'analogue' did not, and the 'free-viewing' vs 'dot probe' categories saw the same pattern of results, respectively. This may indicate stronger overall avoidance of threat for clinical participants and those completing a free-viewing task; however, the difference in sample sizes, and same direction of effect sizes in all categories, suggests these sub-groups may have all reached significance with more studies. In fact, there are multiple other variables that differ between studies, which were not assessed in our analyses. For instance, previous research has found that size of the images presented may impact upon the expression of attention bias (Proulx, 2010). Furthermore, and the age of the faces presented may have had an impact on results. There is research demonstrating a differential expression of attention bias depending on the age of face stimuli presented; for instance, Grossheinrich et al (2018) found a more pronounced attention bias for sad adult faces (compared to child faces), in typically developing children when sad moods were induced. Further studies with large sample sizes are required to further assess the effect of these moderators.

2.4.4. Theoretical implications

The results presented are somewhat in contrast to cognitive models of anxiety, that suggest an early attention bias toward threat is typical of anxious individuals. Thus, these results question whether attention bias towards threat is a 'stable' process underlying anxiety

in young people. Cognitive-motivational models suggest anxiety and attention biases are underpinned by interacting influences from networks of motivational salience-driven and top-down goal-directed factors on a multitude of cognitive processes (such as threat evaluation, attentional switching and orienting, threat inhibition), potentially resulting in a variable ('unstable') expression of attention bias between individuals (Mogg & Bradley, 2018).

Relatedly, and specific to youth, cognitive-learning models suggest that overgeneralised threat evaluation stems from conditioning and cognitive processes related to differential engagement of brain networks across development, which underpins the emergence of maladaptive attention regulation, expressed as variations between initial vigilance, rapid avoidance, sustained threat monitoring, and vigilance-avoidance patterns (Waters & Craske, 2016) – expressions of attention bias that perhaps reflect the combination of multiple processes somewhat unique to individual. From these models, it could be implied that differential development of these maladaptive processes through childhood and adolescence may contribute to the greater variability in attention bias expression found in studies of young people compared to adults. However, it should be noted that within the adult literature there is also considerable variability in results of attention bias across individual studies, yet an anxiety-linked attention bias toward threat does emerge when effect sizes are compiled (Bar Haim et al., 2017; Armstrong & Olatunji, 2012). The discussed models suggest results such as these, from large samples, may reflect the dominant influence of a bottom-up threat-evaluation system over other automatic and controlled orienting processes in the network – a differential influence that only has the power to emerge when samples are large enough (Mogg & Bradley, 2016; 2018). Concordantly, it may be the case that in youth this relative difference in processing has not yet developed such strong or consistent disparity to reflect an orienting bias even when samples are combined.

2.4.5. Clinical implications

Based on relatively robust early findings of an attention bias toward threat in studies of anxious adults (Bar-Haim et al., 2017), attention bias modification (ABM) tasks, initially used to modify these biases in order to test causality, have been increasingly tested in their ability to reduce anxiety symptoms (Linetzky et al., 2015; Lowther & Newman, 2014). This approach has also been tested in anxious young people, mainly using the dot probe task, downwardly extended from adult studies and focused on modifying implicit attention bias towards threat by training attention away from threat at short presentation times. However, results using these training tasks in anxious youth have been mixed, with a recent meta-analysis finding that ABM did not lead to a significantly greater symptom reduction for children or adolescents than a control group (Cristea et al., 2015b). The results from the current meta-analysis suggest that, whilst bias toward threat during initial orienting may characterise anxiety-linked attention in some individuals, it does not appear to be a universal “trait-like” feature of anxiety in youth. Our results suggest strategic avoidance of threat may require greater recognition in attention bias training, but also raise the possibility that maladaptive attentional processes are not reliably expressed in a specific direction. The current meta-analysis results suggest that rather than modify an initial orienting bias for threat it may be valuable to focus on modification of strategic control processes. Some studies have already suggested that ABM reduces anxiety by improving strategic attention control processes (Heeren et al., 2015), and within this, some theorists suggest that visual search tasks may be more appropriate for modifying these voluntary aspects of attention (Mogg & Bradley, 2016). Indeed, in youth, implementations of visual search tasks, where participants search for a benign target (smiling face) from amongst negative distractors (negative faces), has resulted in more consistent symptom reduction (de Voogd et al., 2015; Water et al., 2015).

Furthermore, the likely differential expression of attention bias between disorders/symptoms suggests greater individualisation of ABM tasks to target disorder-specific attention biases may hold some promise.

2.4.6. Recommendations for future research

The moderating effect of anxiety type on attentional maintenance provides a good demonstration of the greater specificity required in future studies by using samples with narrower selection criteria for specific disorders/symptoms. Likewise, including measures of specific developmental factors will allow for more meaningful investigation of *how* age may moderate attention bias.

Improving the ecological validity and disorder-specificity of stimulus displays used in eye-tracking tasks would also help us identify attentional behaviour that may more accurately generalise to real-world environments and therefore more pertinently inform us of attentional processing underlying anxious responses in the real world. This could take the form of more realistic social scenes for some disorders such as social anxiety and could also incorporate the use of video (Gregory, Bolderston, & Antolin, 2018). Taking this further, the use of eye-tracking with interactive video-based tasks may provide even more naturalistic investigations into attentional response to stimuli in situations perceived as evaluative.

Threat intensity and content specificity may also influence expression of attention bias across disorders. Extant research has found attention orienting to be shaped by the intensity of the threat (Bar-Haim et al., 2007). In some adult studies, it appears that as threat level increases so does direction of initial orienting, from vigilance to avoidance and possibly even back to vigilance again (Bar-Haim et al., 2007). Data regarding intensity of threat was not reported in the studies included here, however it may be an interesting avenue for future ET research.

Finally, moving away from rigid vigilance/avoidance constructs may allow for better understanding of anxiety-linked behaviour; over-reliance upon these conceptualisations of attentional deployment may be impeding progress of more accurately identifying other attentional behaviours that underpin anxiety symptoms. For instance, recent studies have identified social anxiety to be linked with vigilance for threat via “hyperscanning”, whereby the individual excessively monitors/scans their surrounding environment (Chen, Thomas, Clarke, Hickie, & Guastella, 2015).

2.4.7. Limitations

This meta-analysis has allowed us to pool the results of multiple studies, however, in comparison to other meta-analyses of attention bias to threat (Armstrong & Olatunji, 2012; Bar-Haim et al., 2007; Dudeney et al., 2015), we had a relatively small number of studies. As a consequence of this some null results may have been due to low power. The relatively low number of studies included also prevented some moderator analyses from being carried out. Additionally, a number of studies that were eligible for inclusion were excluded due to inadequate and unavailable data to compute an effect size.

Attention is known to be a temporally dynamic process, and the wide variation in display times used (ranging from 1250ms to 10,000ms) but a lack of power to conduct meta-regression on these potential moderating factors, means results of an avoidance bias must be taken with caution. Similarly, the number of studies included prevented meta-regressions for potentially meaningful moderators such as age and gender. Finally, there was limited heterogeneity of the variance in the two between-group meta-analyses, but moderator analyses were run based on a-priori statistical planning. However, this does mean there was limited variance to be explained between effects sizes that wasn't due to random sampling error, and as such any moderator results should be interpreted with caution. Nevertheless, the

results of this meta-analysis still provide insightful results regarding the expression of attention bias in young people with and without anxiety.

2.4.8. Conclusions

In contrast to adult studies, results from these meta-analyses suggest that anxious and non-anxious youth do not differ in overt initial orienting to threat, as measured by eye movements; however, our results do demonstrate a small effect suggesting anxious youth are more likely to avoid maintaining attention on threat. Future research with large sample sizes and use of time-windows is required to investigate the pattern of strategic attention across time more discretely. Multiple variables demonstrated potential to moderate outcome, suggesting future research is required to delineate the factors contributing to the individual differences found in attention bias expression amongst anxious youth.

Chapter 3

A version of this chapter is published as:

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3

Multi-session Cognitive Bias Modification: Targeting multiple biases in adolescents with elevated social anxiety

Research studies applying Cognitive Bias Modification of Attention (CBM-A) and Interpretations (CBM-I) training to reduce adolescent anxiety by targeting associated cognitive biases have found mixed results. This chapter presents a new multi-session, combined bias CBM package, which uses a mix of training techniques and stimuli to enhance user-engagement. We present preliminary data on its viability, acceptability and effectiveness on reducing symptoms and biases using an A-B case series design. Nineteen adolescents with elevated social anxiety reported on their social anxiety, real-life social behaviours, general anxiety, depression, and cognitive biases at pre/post time-points during a two-week baseline phase and a two-week intervention phase. Retention rate was high. Adolescents also reported finding the CBM training helpful, particularly CBM-I. Greater reductions in social anxiety, negative social behaviour, and general anxiety and depression, characterised the intervention but not baseline phase. There was a significant correlation between interpretation bias change and social anxiety symptom change. Our enhanced multi-session CBM programme delivered in a school-setting appeared viable and acceptable. Training-associated improvements in social anxiety will require further verification in a study with an active control condition/group.

3.1. Introduction

Social anxiety is prevalent in youth (Wittchen, Stein & Kessler, 1999), can disrupt academic performance and interpersonal interactions (Owens, Stevenson, Norgate, & Hadwin, 2008), persist into adulthood, and impact other disabling mental health conditions and quality of life (Woodward & Fergusson, 2001). Cognitive Behavioural Therapy (CBT), the current gold-standard treatment can reduce social anxiety in youth (Scaini, Belotti, Ogliari, & Battaglia, 2016) but many fail to show clinically significant responses (Kendall, Settipani, & Cummings, 2012), respond but subsequently relapse (Ginsburg et al., 2014), or find it difficult to access. Identifying more effective, accessible methods so that young people can better manage their symptoms is a public health priority. Cognitive bias modification (CBM) training, which uses computerised tasks to target symptom-linked cognitive biases, has emerged as a potential adjunctive intervention (Butler et al., 2015; White et al., 2016) that may be amenable to delivery through computerised formats at home (Salemink, Kindt, Rienties, & Van Den Hout, 2014) or in school (Fitzgerald, Rawdon & Dooley, 2016). Yet, existing CBM packages remain weak at boosting more adaptive information-processing styles and at reducing symptoms (Cristea et al., 2015a; Cristea et al., 2015b; Heeren et al., 2015; Mogoșe et al., 2014). This study presents a newly developed, multi-session computerised training program that targets multiple cognitive biases using a variety of training techniques and stimuli, for adolescents with elevated social fears. We assess the viability of administering this training tool at school, its acceptability to young people and compare changes in biases and symptoms across a baseline and an intervention phase.

Drawing on cognitive models of social anxiety (Clark & Wells, 1995; Rapee & Heimberg, 1997), a large corpus of research has found a link between social anxiety and attention and appraisal biases in adults as well as adolescents (Bar-Haim et al., 2007; Haller et al., 2016; Klein et al., 2017; Miers et al., 2008; Rheingold, Herbert, & Franklin, 2003). These are suggested to manifest as: greater allocation of attention to threatening stimuli at

involuntary and voluntary stages of processing (Roy et al., 2008; Stirling et al., 2006); a tendency to interpret ambiguous cues in threatening ways; and a tendency to disproportionately attribute negative events as caused by oneself (i.e., ‘internal’ reasons) and positive events as caused by others or circumstance (i.e., ‘external’ reasons). Computerised cognitive training methods, which encourage more adaptive styles of information-processing over repeated trials and practice, have been developed in adults to reduce general and social anxiety. Cognitive Bias Modification of Attention (CBM-A¹) methods alter maladaptive attention-orienting patterns towards threat and encourage selective attention towards neutral or positive stimuli. Most commonly, CBM-A methods use a modified dot probe task in which probes only ever appear in place of non-threatening stimuli (MacLeod, Mathews, & Tata, 1986). In contrast, in ‘visual search’ CBM-A training the individual must locate a non-threatening stimulus from among threatening stimuli as quickly as possible (Waters et al., 2007). Cognitive Bias Modification for Interpretations (CBM-I) targets biases in interpretation, mostly using the ‘ambiguous situations task’ (Mathews & Mackintosh, 2000). Here, participants read a series of ambiguous sentences that end with a word fragment. Completion of the final word disambiguates the valence of the sentence in a positive direction. Participants receive a follow-up ‘yes/no’ comprehension question with ‘correct/incorrect’ feedback in order to reinforce the training. A few studies have developed programs to modify attributions in adults to reduce depressive mood (Peters, Constans & Mathews, 2011) but not anxiety.

However, studies of adults with various anxiety conditions (including trait anxiety) have only found weak (but significant effects) in symptom change (Hakamata et al., 2010; Hallion & Ruscio, 2011; Heeren et al., 2015, but also see: Cristea et al., 2015a; Mogoase et al., 2014). Reduction in symptoms typically occur when there is also successful bias

¹ This chapter refers to Cognitive Bias Modification for Attention as CBM-A in order to retain clarity of description when discussing CBM-A together with CBM-I as part of an overarching CBM training method. CBM-A referred to here is conceptually identical to Attention Bias Modification (ABM) discussed in the rest of the thesis.

modification (MacLeod & Clarke, 2015), and possibly through multiple training sessions (Hallion & Ruscio, 2011). Extensions of CBM-A and CBM-I for use in adolescents (Bar-Haim, Morag, & Glickman, 2011; Lau, Belli & Chopra, 2013), using the same tasks but with modifications to the stimuli content and modality (audio/text/pictures) have found small to medium effects of CBM-I and CBM-A training on cognitive biases, but no effect on general indices of mental health (nor on anxiety specifically) (Cristea et al., 2015b). Looking at these packages separately, Lowther & Newman (2014) identified that 8 out of 10 CBM-A studies reported positive changes in anxiety post-intervention (although only 4 of these 8 studies also found a change in attention bias). Through a meta-analysis, Krebs and colleagues (2017) found that CBM-I had a statistically significant moderate effect on decreasing negative interpretations and boosting positive interpretations. A small but significant effect on self-reported anxiety immediately following training was also found. While adult studies have tried to alter cognitive processes relating to depression through attribution training (Peters, Constans & Mathews, 2011), their extension to young people has focused on targeting aggressive behaviours and academic achievements (Sukariyah & Assaad, 2015; Vassilopoulos, Brouzos & Andreou, 2015). No studies to our knowledge have trained adaptive attributions in adolescents (or adults) to reduce anxiety. Thus, while CBM training packages have potential, efforts to boost bias change and symptom reduction are needed. Adult data advocate multi-session training but their extension to anxious adolescents yield mixed findings regarding symptom and bias change for CBM-A (de Voogd et al., 2016; de Voogd, Wiers & Salemink, 2017b; Fitzgerald, Rawdon & Dooley, 2016; Pergamin-Hight et al., 2016) and CBM-I (de Voogd et al., 2017a; Reuland & Teachman, 2014). Therefore, consideration of other methodological factors may be important in prompting significant symptom change.

The current study aimed to improve CBM training effects by incorporating several methodological features into the training package. Some of these features drew directly on

findings around known contributions of cognitive factors to anxiety, while others aimed to increase user-engagement. Consistent with combined cognitive bias hypotheses of psychopathology (Everaert, Duyck & Koster, 2014; Everaert, Koster & Derakshan, 2012; Hirsch, Clark & Matthews, 2006), we first included bias modification procedures to target both attention and interpretation biases in social anxiety, within the same package. Targeting biases together may produce a greater magnitude of change (because of their combined additive and interactive effects). Only one study we are aware of has utilised a combined-bias approach in socially anxious adolescents (de Hullu et al., 2017; Sportel et al., 2013), testing an internet-based CBM-A/CBM-I program and finding significant improvement across all groups but no significant difference between internet-based CBM, CBT and control group. Secondly, CBM-A tasks aim to modify maladaptive processes of selective attention towards, and difficulty disengaging from, threatening environmental stimuli, yet do less to target self-focused attention. Models of social phobia (Clark & Wells, 1995) posit that the socially-anxious individual shifts their attention inwards to produce an (often negative) image of themselves, based on interoceptive sources, rather than actual monitoring of others' responses to disconfirm these negative fears. This self-focused attention in turn reduces processing of environmental cues in adults as well as adolescents (Hodson, McManus, Clark & Doll, 2008; Judah, Grant & Carlisle, 2015), which suggests that targeting these maladaptive self-focused attentional processes during CBM-A training could be beneficial (Wells & Papageorgiou, 1998). We therefore included a task within the CBM-A package that draws the individual's attention toward their internal feelings and then encourages them to shift their attention externally to stimuli that challenge these beliefs of how others view them in a social situation. Thirdly, we also increased the scope of CBM-I by targeting attribution biases too, particularly the tendency to internally attribute responsibility for negative events compared to positive events (Haller et al., 2016). We included a second task within the CBM-I package, that asked young people to generate an internal attribution for a positively interpreted event.

Finally, trial repetition, boredom and disengagement are serious concerns for CBM training (Beard, 2011). We increased user-engagement by varying the training techniques used and the modality of stimulus presentation. A combination of CBM-A techniques was used, from the dot probe to the visual search tasks. In the dot probe, we trained attention towards positive words and faces on some blocks, and attention towards neutral words and faces on other blocks - always away from negative stimuli. In the visual search, participants identified a smiling face from a grid of negative faces in one module, but also practiced shifting their attention from internal sensations and cues toward benign, external interpersonal cues in another module. For CBM-I, we used text-based scenarios to encourage benign/positive resolution of ambiguous situations, as well as visual presentations of ambiguous scenes that had to be resolved benignly/positively. The latter may allow for more effective visualisation, and therefore stronger emotional responses and bias modification, than material presented in word form (Holmes et al., 2006; Holmes & Matthews, 2010).

To assess viability and acceptability of our enhanced, multi-session CBM intervention for social anxiety, we used an A-B case series design, in which adolescents selected for high social anxiety received 8 school-based CBM training sessions, in two 4-day blocks over a 2-week period. We also gathered quantitative data on changes on selected measures during the two-week intervention phase but also during a 2-week baseline period. We expected a significant decrease in social anxiety symptoms, and a significant change in attention and interpretation biases. Due to these clear a priori hypotheses, we conducted significance testing on changes in social anxiety symptoms, real-life socially avoidant behaviour and measures of attention and interpretation biases during the baseline versus the intervention phases. We also calculated the correlation between changes in social anxiety and changes in cognitive measures. To explore specificity effects to social anxiety symptoms, we measured changes on general anxiety and depression symptoms.

3.2. Methods

3.2.1. Design

A single case series A-B design was used. Participants completed a 2-week baseline phase, followed by a 2-week intervention phase. Individual baselines acted as control periods to allow us to compare the effects of administering the CBM programme on symptom and bias measures against any natural fluctuations over time. Self-reported measures of social anxiety, general anxiety, mood/depression, cognitive biases and responsiveness to real-life stressors were assessed before and after the 2-week multi-session CBM program, and also before and after the 2-week baseline phase, in which no training took place - resulting in 4 assessment time-points. As this study was carried out in secondary schools the procedure was designed to fit in with students' schedules. Therefore, the pre-baseline phase assessment took place on the first Monday of the study, with the post-baseline phase assessment taking place on the Friday of the following week, 12 days later. After a 2-day break for the weekend, the pre-training phase assessment took place on the following Monday. Finally, the post-training phase assessment was carried out on the Friday of the following week, 12 days later. The use of 4 assessment time-points allowed for the comparison of pre-post changes over two distinct phases, one of which involved the CBM intervention. As the baseline and intervention phases were matched for duration, degree of change across pre/post assessment sessions could be directly compared within-subjects. See Figure 3.1 for an illustration of the study timeline.

3.2.2. Participants

Adolescents aged 16-18 years were recruited from two secondary schools in South London, England. Using an opt-out procedure, seventy-eight students (65 females and 13 males) completed the pre-screening Social Anxiety Scale for Adolescents (SAS-A). As teachers passed the information onto pupils and only those who were interested in taking part

attended the screening session, it was difficult to calculate the initial recruitment rate and/or to assess the representativeness of those who did the screening. Using the recommended clinical cut-off of 50 (La Greca & Lopez, 1998), 25 students (24 females) were invited to take part in the 4-week study. 22 females and 1 male agreed to participate but 4 of these dropped out prior to study completion, due to existing time commitments at school, leaving 19 participants who completed all training and assessment sessions (18 females and 1 male). Given that this study aimed to explore the preliminary effects associated with a multi-session, multi-bias enhanced CBM training program in adolescents, there were no prior studies upon which to base sample size calculations. Furthermore, the need for a priori power calculations for case series designs has been debated. Our final sample size was commensurate with the mean/median of other case series in the literature (Abeles et al., 2009; Bechor et al., 2014; Blackwell & Holmes, 2010; Rozenman, Weersing, & Amir, 2011). We did not conduct a formal assessment of current and lifetime mental health diagnoses. Current mental health diagnoses were listed as an exclusion criterion in our information sheets and the participant was asked to confirm during the consenting procedure that they had no current or lifetime diagnoses and had never received treatment from a mental health service. As all participants were over 16 years, they provided informed consent. Ethical approval for this protocol was granted by the Psychiatry, Nursing & Midwifery Research Ethics Subcommittee, King's College London (PNM/13/14-157). Sample characteristics and self-report scores on symptoms measures appear in Table 3.1.

Table 3.1. Sample Characteristics and Mean (Standard Deviation) of SAS-A, MFQ and SCARED at the four assessment points

Time-point	Baseline Phase		Training Phase	
	Pre	Post	Pre	Post
Session	Assessment 1	Assessment 2	Assessment 3	Assessment 4
N	19	19	19	19
Age (Years)	17.03			
Social Anxiety Score (SAS-A)	63.68 (8.08)	63.05 (8.46)	62.74 (8.23)	58.32 (10.23)
MFQ – Total Score	29.53(13.02)	32.63 (13.14)	29.84 (12.27)	22.47 (10.82)
SCARED – Total Score	42.68 (12.91)	43.53 (10.78)	40.58 (11.93)	35.74 (13.53)

Note: SAS-A = Social Anxiety Scale for Adolescents; MFQ = Mood and Feelings Questionnaire; SCARED = Screen for Child Anxiety Related Disorders.

3.2.3. Procedure

For an illustration of the study phases see Fig 3.1. Both the 12-day baseline and intervention phase consisted of two (pre/post) assessment sessions, each lasting approximately 45 minutes but with the pre/post assessment sessions of the intervention phase either side of a block of eight CBM training sessions (each lasting around 15-20 minutes, and never longer than 30 minutes). Approximately 4-weeks after the initial screening, each participant was seen individually in a quiet classroom, supervised by a researcher, throughout each session of data collection, including the CBM training. During Assessment 1, on the first Monday of the baseline phase, participants completed questionnaires on social anxiety, general anxiety and depression symptoms, followed by cognitive bias measures. During this week participants were also asked to complete the Social interaction diary at the end of the day on Tuesday-Thursday, and email the responses to the researcher each evening. The questionnaires and cognitive bias measures were repeated for Assessment 2, the post-baseline assessment, on the Friday of the following week. On the following Monday, these measures were repeated again for Assessment 3, the pre-training assessment. Training sessions 1-4 were carried out on the Tuesday-Friday of the same week, and saw the participant complete one interpretation training task per day from the training program. The following Monday-

Thursday consisted of training sessions 5-8, which saw the participant complete one attention training task per day from the training program. As the interpretation training was anticipated to be more engaging (based on adult findings - Beard, Weisberg, and Primack (2012)), we hoped we would retain more participants by administering it first. During Assessment 4, on the Friday of the same week, participants completed the same battery of measures from the previous assessments to provide us with a post-training assessment. The week after the final session, participants were again asked to complete the social interaction diary at the end of the day on Tuesday-Thursday, and email the responses to the researcher each evening. At the end of the entire study each participant was provided with full debriefing.

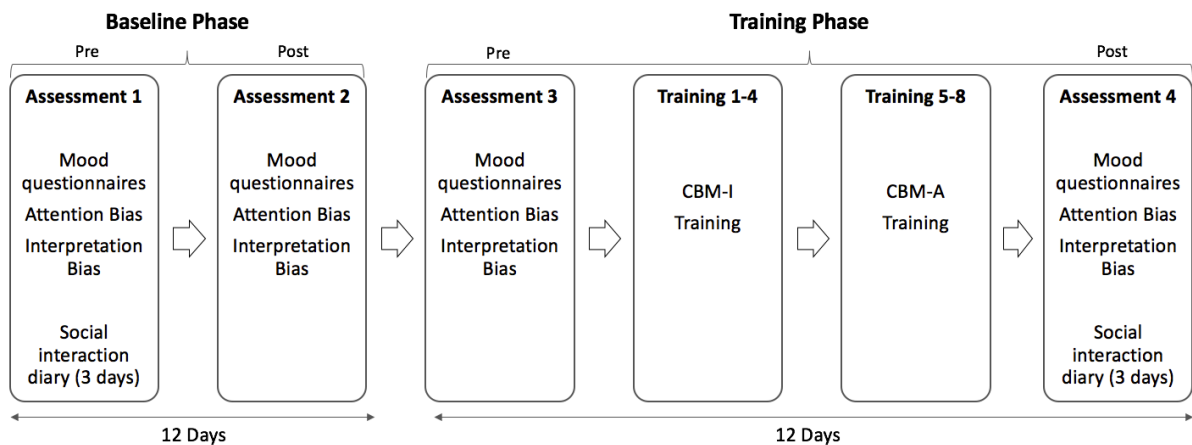


Fig 3.1. Schedule of assessment and training sessions for each participant.

3.2.4. Materials

Enhanced CBM Training Intervention

CBM-I: Interpretation and Attribution Training

This training segment consisted of 4 sessions - two of these used written vignettes to describe ambiguous social scenarios and two used picture scenes in an attempt to increase the vividness of ambiguous scenes (see Figure 3.2). All picture stimuli used was from Haller et

al., (2016, 2017) in which a new, picture-based tool was developed to measure interpretational and attributional biases of visual social cues in adolescents. The social situations used were based upon several previous adolescent CBM-I studies (Lau, Belli & Chopra, 2013; Lothmann et al., 2011). During all interpretation training tasks participants were trained to endorse positive/benign rather than threatening interpretations in response to presentation of ambiguous, age-appropriate social scenarios. Session 1 presented participants with 25 text-based ambiguous situations that each ended with a word fragment in a positive or benign direction. Participants were asked to complete each fragment by typing in the correct letter. Correct completion disambiguated the scenario and a comprehension question followed, designed to reinforce the interpretation. For half of the comprehension questions, the correct answer was ‘yes’ and for the other ‘no’, so that they were not always positive. This was followed by a “correct/wrong” message. Session 2 was largely equivalent, but first used a picture scene to increase the vividness of the situation, which was then followed by a text-based description, with word fragment to complete, and comprehension question. As with the written descriptions in session 1, the initial picture scene presented to the participant in session 2 was always ambiguous. The text-based description with the word fragment after the picture was then designed to disambiguate the social scene in a benign or positive direction. Sessions 3 and 4 were identical to Sessions 1 and 2, but at the end of the interpretation component an additional question about attributions was posed to encourage participants to generate an internal attribution for the positively interpreted event. For instance, as outlined in Figure 3.2, after training the participant to interpret an ambiguous event (approaching a group of friends waiting to chat with them) in a positive direction, they are then asked a question based upon this event (“What makes you good to talk to?”), encouraging them to attribute this positive outcome toward their own internal characteristics. This was an open response question in which the participant typed an answer using the keyboard. All sessions presented 25 interpretation trials.

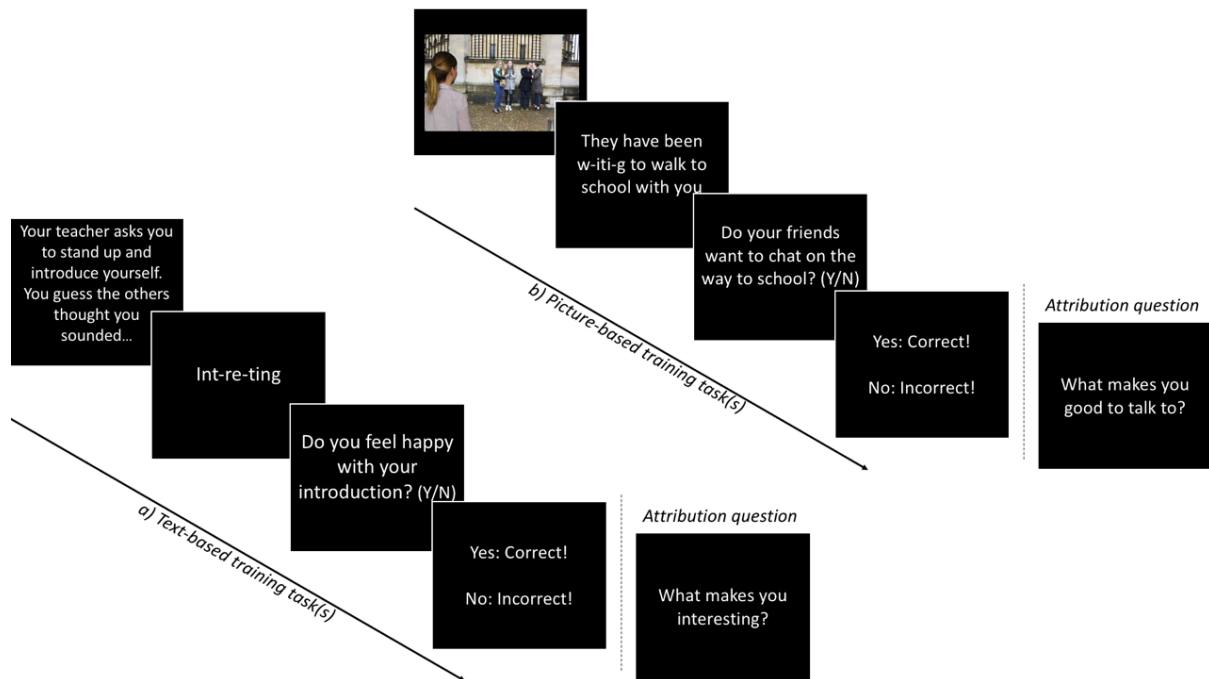


Fig. 3.2. CBM-I Training tasks: Sequence a) illustrates the text-based interpretation training tasks, with additional attribution question used in the attribution task variant. Sequence b) illustrates the interpretation training tasks using picture scenes.

CBM-A: Attention Training

Of the four attention training sessions, two used the dot probe task, and two used the visual search task. Figure 3.3 outlines each task.

Dot probe task. Of the dot probe training sessions, one session used emotional faces while the second session used emotional words (see Figure 3.3). We supplemented threat-neutral pairings with threat-positive pairings, to encourage attention towards positive stimuli, making it more commensurate with the visual search task. Emotional adolescent face stimuli (neutral, angry, happy) were used from the NIMH Child Emotional Faces Picture Set (NIMH-ChEFS; Egger et al., 2011). Participants viewed 160 trials (4 blocks of 40 trials) during each training session. Of these 64 were angry-neutral, 64 were angry-happy and 32 were neutral-neutral filler trials (interspersed to reduce chances of habituation to the

expressions). Eight female and eight male faces were used. Each face pairing used the same actor. Each face pairing was shown four times for Angry-Happy and Angry-Neutral trials and twice for Neutral-Neutral trials. Each face photograph subtended 45mm in width and 34mm in height. The face photographs were presented with equal distance to the left and right of the fixation cross, with a distance of 14mm between them. Each trial began with the presentation of a fixation display for 500ms (white cross 1*1 cm at the centre of the screen), on which the participants were requested to focus their gaze. The fixation display was followed by a face pair display for 500ms, immediately followed by a target probe (“p” or “q”); consistently in the location of the neutral or happy stimulus. Participants were required to locate the probe position and determine which symbol appeared by pressing one of the two pre-specified keys on the keyboard. The target remained on the screen until the participant responded. This meant that we were targeting attention biases at both voluntary and involuntary stages of processing, consistent with findings that anxiety symptoms have been associated with both (Lau & Waters, 2017). An inter-trial-interval (500ms) followed, before the next trial. A short break was given every 40 trials. Trials were presented in a randomised order. For session 2, the dot probe word training task, participants viewed 160 trials; 64 Negative-Neutral, 64 Negative-Positive and 32 Neutral-Neutral socially relevant word pairings. 8 words were used 4 times each in the Negative-Neutral and Negative-Positive trials, and twice each the Neutral-Neutral Trials.

Visual Search. This training paradigm again consisted of two sessions (see Figure 3.3). Participants completed one session of visual search within a grid (based on Waters et al., 2013), in which they were required to repeatedly identify the only positive (smiling, mouth open) face in a 3 x 3 matrix of negative (angry, mouth closed) emotional faces. The faces used in this task were the same faces used in the dot probe training. In the second session of visual search, they were presented with a relevant social scene, in which they were required

to repeatedly identify a specified non-threatening face, along with questions designed to reduce self-focused attention and perspective taking to this external cue. The stimuli for this new task was also taken from Haller et al., (2016, 2017). We consciously chose stimuli that was not overly positive (relatively ambiguous), to attempt to mirror real-world situations the participant may encounter. After directing them to focus on their self-focused attention in response to this social-scene, we then prompted them to shift their attention externally to non-threatening stimuli in the social scene, that challenges their potentially negative beliefs of how others view them.

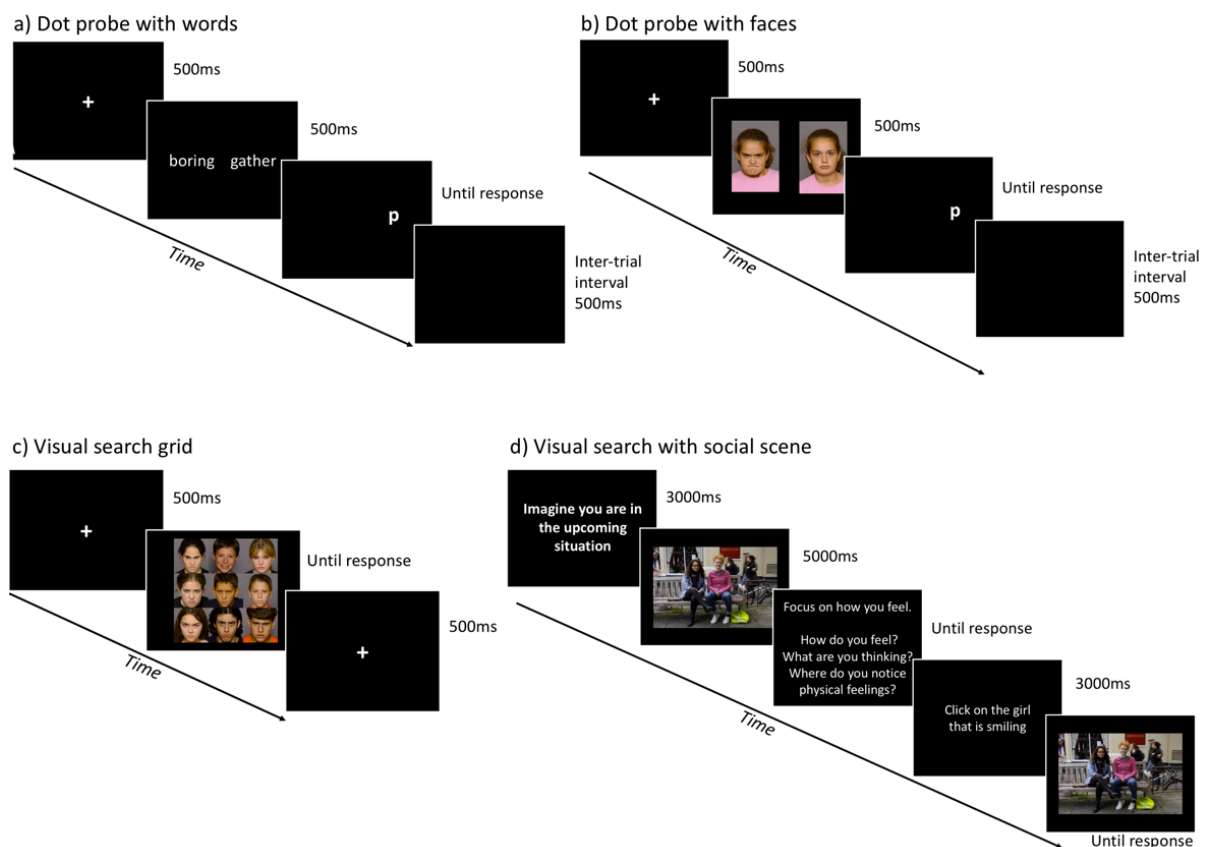


Fig. 3.3. Sequence of stimuli presentation for each of the four attention training tasks

Self-report symptom measures

Questionnaire and diary measures assessed pre and post social anxiety symptoms and social interactions. The primary symptom measures were self-reported social anxiety and

social interaction ratings. Measures of self-reported general anxiety and depression were collected to assess whether training effects were specific to social anxiety or had more general effects.

Social anxiety

Social anxiety was measured using the Social Anxiety Scale for Adolescents (SAS-A; La Greca & Lopez, 1998), a 22-item self-report measure of social anxiety symptoms. For the present study, internal consistency was $\alpha = 0.81$ (using assessment 1 data), with test-retest reliability (using assessments 1 and 2 at baseline) at $r = 0.86$.

Social Interactions

This newly developed measure allowed participants to rate anxiety levels in response to real-life negative events using a self-report Visual Analogue Scale (VAS). Participants were asked how many negative interactions they experienced each day, to rate how “upset” or “angry” they felt immediately following their most negative interaction each day, from 0 (not at all) to 7 (extremely), and how “upset” or “angry” they subsequently felt (0-7). They were also asked to indicate how many potential social interactions they avoided each day. This questionnaire was provided as an email to the participant and treated as a “diary” to complete and return at the end of each day for 3 days (Tuesday-Thursday) during the first week of baseline phase, and 3 days (Tuesday-Thursday) the week following the training phase.

General anxiety

Anxiety symptoms across dimensions of anxiety were measured using the Screen for Child Anxiety Related Disorders (SCARED; Birmaher et al., 1999), a 41 item self-report

measure. For the present study, internal consistency was $\alpha = 0.89$ (using assessment 1 data), with test-retest reliability at $r = 0.91$ (using assessments 1 and 2 at baseline).

Depression

Depression was measured using the Mood and Feelings questionnaire (MFQ; Costello & Angold, 1988). For the present study, internal consistency was $\alpha = 0.92$ (using assessment 1 data), with test-retest reliability at $r = 0.83$ (using assessments 1 and 2 at baseline).

Cognitive bias measures

Interpretation bias

Adolescent Interpretation bias task (AIBT; Heathcote et al., 2016). This task consists of a series of incomplete vignettes describing ambiguous situations relevant to adolescent life. The task was originally created to investigate interpretation bias and the experience of pain in adolescents, and therefore consists of 8 vignettes relating to social situations and 8 relating to bodily threat. Only data from the social situations items were used for this study. After each vignette, the participants are presented with two different possible endings (negative or positive), which they must rate in terms of whether or not that interpretation popped into their mind, on a scale of 1 to 5. Finally, participants are asked to select the interpretation that most readily popped into their mind. They then see all the situations again, but this time must rate them based on their *belief* that each interpretation would actually be happening in that situation. Participants' mean interpretation bias scores were calculated by subtracting total ratings of negative endings from total ratings of positive endings, when asked how likely the interpretation was to pop into their mind. A negative score indicates a bias toward negative interpretations. As our focus for this measure was on interpretation bias, we used the 'likelihood' rating scores as this was most commensurate with other measures of

interpretation bias (Amin, Foa, & Coles, 1998; Fu et al., 2013; Miers et al., 2008). However, changes on the ‘belief’ questions and on forced choice questions during the baseline and intervention phases were similar to those reported for the likelihood ratings, and are available from the first author on request. For the present study, test-retest reliability (using assessments 1 and 2 at baseline) was $r=0.88$.

Attention Bias

Dot probe task. The design of this task mirrored that used for the CBM-A training phase. This assessment task consisted of 160 trials: 80 trials of word stimuli, followed by 80 trials of face stimuli (32 neutral-angry trials, 32 neutral-happy trials and 16 neutral-neutral filler trials). The probe appeared with equal probability behind the emotional and neutral stimulus. Raw reaction time data for each participant was analysed (separately for words and faces) and trials with a response time ± 3 standard deviations for the participant’s mean were eliminated from further analyses (2.1% of all words trials, 1.8% of all faces trials). Trials with incorrect responses were also excluded (6.8 % of all words trials, 6.5% of all faces trials). Participants who made incorrect or outlying responses on greater than 25% of trials were excluded from subsequent analyses. Following this, an attentional bias score was computed for each trial-type (Bias Score = ProbeNeutral - ProbeEmotion). Positive bias score values indicate a bias towards the emotion (vigilance bias) and negative values indicate a bias away from the emotion (avoidance bias). This was conducted separately for the dot probe task using word stimuli and dot probe task using face stimuli. Participants with an extreme bias score (± 3 standard deviations from the overall group mean) were excluded, resulting in the exclusion of one participant’s data from the dot probe analyses. Based on our study aims, our results focus only on vigilance/avoidance of threat (i.e. Neutral-Threat trials). For the present study, test-retest reliability (using assessments 1 and 2 at baseline) was $r=-0.01$.

Feedback questionnaire

At Assessment 4, participants were asked for their views of the program: “what were the most help/unhelpful aspects of the program?”; “which parts of the program did you find the most enjoyable/unenjoyable?”; “do you have any other comments on the program?”.

Viability and Feedback

We assessed viability and participant acceptability by monitoring recruitment and drop-out rates. Responses to the feedback questions were collated into a database and salient themes were identified.

3.2.5. Quantitative data

Questionnaire total scores were calculated at 4 times points; pre- and post-baseline phase (Assessment 1 and 2), and pre- and post-training phase (Assessment 3 and 4) for each individual and are presented in Table 3.4. Due to a priori hypotheses, we performed statistical tests of the degree of change during the baseline versus intervention phase. These scores were entered into a 2x2 ANOVA with Phase (baseline and training) and Time (pre, and post) as the two within subject variables. Results of the self-report social interaction diary were collated; ratings of negative social interactions, immediate emotional response to the most negative interaction and number of social situations avoided over the days preceding the training program (during baseline) and the days following training (during the intervention) were again presented for all individuals. Paired samples t-tests were used to compare these pre- and post-assessment measures. Similarly, interpretation bias scores were presented for all 4 assessment time-points, and also entered into a 2x2 ANOVA with phase (baseline and training) and time (pre and post) as the two within subject variables. Attention bias scores for Neutral-Threat trials were also presented for each individual at all 4 assessment time-points

and entered into a 2x2 ANOVA with phase and time as the two within subject variables. This was completed separately for words and faces conditions. A bivariate correlation analysis between change of attention bias, change of interpretation bias and change of symptoms (all Assessment 3 - Assessment 4) is also presented. Bonferroni adjustment controlled for type 1 error in analyses where multiple ANOVAs were conducted, with adjusted p-values reported.

3.3. Results

3.3.1. Descriptive data and baseline associations

Mean scores for participants on questionnaire symptom measures of social anxiety, general anxiety and depression at each assessment are presented in Table 3.1. Table 3.2 reports correlations between cognitive bias measures with each other and with social anxiety symptom scores at baseline. None of these correlations reached significance.

Table 3.2. Correlations (r) between social anxiety scores on SAS-A and cognitive bias measures at baseline.

<i>Measure</i>	<i>AIBT</i>	<i>Dot probe Words</i>	<i>Dot -Probe Faces</i>
SAS-A	-0.356	-0.381	-0.316
<i>Significance (p)</i>	0.134	0.119	0.202
AIBT		0.385	0.093
<i>Significance (p)</i>		0.115	0.714
Dot probe Words			-0.004
<i>Significance (p)</i>			0.986

Note: SAS-A = Social Anxiety Scale for Adolescents; AIBT = Adolescent Interpretation Bias Task (bias score); Dot probe Words = Dot Probe bias score with word stimuli; Dot probe Faces = Dot probe bias score with face stimuli. Negative Dot Probe bias scores indicate an avoidance bias (toward neutral); negative AIBT bias scores indicate a proclivity toward negative interpretations.

3.3.2. Viability and Feedback

19 of the 23 participants completed the full CBM program - a retention rate of 82.6%. Salient themes were identified from participant feedback responses: 67% of participants expressed that they found the social situations tasks generally felt helpful, with 45% claiming

they thought the social situations task helped them in viewing situations more positively/less negatively. 33% of participants indicated they found the dot probe tasks unhelpful, with the remaining 67% consisting of mainly "N/A responses. A full list of feedback responses can be found in Table 3.3.

Table 3.3. Qualitative feedback from participants regarding their experience of the CBM training program.

Participant	Feedback
1	Felt it helped realise that not every situation should be interpreted negatively. Dot probe task didn't feel helpful or enjoyable. Liked having to imagine themselves in certain situations, and try to think positively about them.
2	Felt that being given a "correct answer" for the visual scenarios kind of made them rethink their interpretation of the situation.
3	Felt they were able to think more positively about situations after training.
4	Enjoyed the situations task and found it helpful seeing them in a different more positive angle after a while. Preferred the descriptions to pictures. At some points it felt too long, especially on dot probe task. It was pretty easy to understand and follow and helped them think about situations more positively.
5	They felt the interpretation bias tasks with pictures were helpful. In fact, the whole "situations" part of the programme felt helpful. They didn't feel like the dot probe tasks felt like they were helping in any way.
6	Thought it was all "ok".
7	Didn't feel like it was helpful.
8	Felt the part where they had to look at how others perceived them was helpful. The dot probe task felt pointless. They liked the fact it was computerised and there wasn't too much one on one talking. The dot probe tasks were quite confusing.
9	They felt it possibly allowed them to view social situations in a more positive way. The sessions were long. The tasks themselves were very boring and repetitive. They felt the programme itself does not help to reduce the way they view social situations but now the aim has been more thoroughly explained they may begin to view their own social interactions differently, more positively. Felt the word-based scenarios allowed them to better imagine themselves in the situation than the pictures.
10	Didn't enjoy answering the open questions.
11	The social situations task felt helpful.
12	The questionnaires made them question why they have been stressing so much. They feel they have become much more calm, especially coming to school, because they

- would usually be nervous about the day in general before coming in. Didn't see the point in the dot probe task.
- 13 Felt it was helpful when imagining different scenarios to see how they would react to them. Enjoyed the detecting the smiles game (visual search). Felt the scenarios were too repetitive.
- 14 Felt imagining themselves in situations was helpful. The dot probe task didn't feel beneficial.
- 15 Thought the tasks should be shorter.
- 16 Felt the social scenario tasks were helpful. Thought the picture-based scenarios were less helpful than the word-based ones.
- 17 Thought it was beneficial to realistically look at how certain scenarios won't play out as badly as they think.
- 18 They found the social scenario questions useful in relating them to the reality of decision making. They found the tasks very simple and straightforward to understand.
- 19 It helped them realise that not every situation should be interpreted negatively. The dot probe task didn't feel helpful or enjoyable. Enjoyed imagining themselves in certain situations and trying to think positively about them. Felt some of the tasks lasted too long.

Note: Participants were asked "Were there any aspects of the program that you found particularly helpful/unhelpful?", "Were there any aspects of the program that you particularly liked/disliked?". The responses above are a collation of these answers.

3.3.3. Quantitative data

Quantitative data: Individual Questionnaire Scores. Each participants' scores on the social anxiety, general anxiety and depression symptom measures at the four assessment time-points are displayed in Table 3.4. Individual participants' scores on the social interaction diary items are displayed in Table 3.5.

Table. 3.4. Sample Characteristics and total SAS-A, MFQ and SCARED scores for each participant at Assessment 1 (pre-baseline phase), Assessment 2 (post-baseline phase), Assessment 3 (pre-training phase) and Assessment 4 (post training phase).

Participant	Age	Sex	Baseline Phase						Training Phase					
			Assessment 1 (Pre)			Assessment 2 (Post)			Assessment 3 (Pre)			Assessment 4 (Post)		
			SAS-A	SCARED	MFQ	SAS-A	SCARED	MFQ	SAS-A	SCARED	MFQ	SAS-A	SCARED	MFQ
1*	18.00	F	47	32	27	49	35	21	47	23	16	43	20	21
2	17.25	F	62	42	28	63	38	32	60	30	36	64	31	38
3	16.58	F	60	37	18	60	36	23	60	34	22	64	38	23
4	16.75	F	63	33	18	56	37	24	51	38	15	57	35	13
5*	16.83	M	63	52	30	68	51	28	66	52	31	59	49	39
6	16.58	F	74	61	43	76	57	49	69	55	34	75	49	37
7	16.67	F	83	56	27	84	53	32	83	51	28	85	51	39
8*	16.75	F	59	39	24	62	44	39	60	34	35	54	37	23
9*	17.33	F	68	43	15	63	48	17	63	35	13	46	29	2
10*	17.25	F	63	25	15	60	29	15	60	24	19	59	27	14
11*	17.92	F	58	64	45	56	65	38	63	66	46	56	54	25
12*	16.33	F	66	44	37	67	49	48	66	41	16	62	30	19
13	17.08	F	53	17	13	59	34	31	58	29	37	58	15	10
14*	16.75	F	59	35	22	58	39	29	58	39	37	51	32	21
15*	16.92	F	58	36	33	56	31	30	61	37	34	52	15	20
16*	16.92	F	75	49	59	75	44	60	77	43	60	68	47	31
17*	17.00	F	68	31	24	56	27	12	56	31	18	48	18	6
18*	17.92	F	65	58	29	69	59	39	67	57	29	59	60	23
19*	16.75	F	66	57	54	61	51	53	67	52	41	48	42	23

*Note: SAS-A = Social Anxiety Scale for Adolescents; MFQ = Mood and Feelings Questionnaire; SCARED = Screen for Child Anxiety Related Disorders. *Individuals for whom social anxiety scores showing a reduction from assessment 3 to 4.*

Table 3.5. Mean scores on the social interaction diary items, for each participant pre and post training.

Participant	Pre -Training			Post-Training		
	Negative Interactions	Situations Avoided	Emotional Response	Negative Interactions	Situations Avoided	Emotional Response
1	0.5	0.5	3	1	1	5
2*	3	2	3	0.5	1.5	1.5
3	0.5	0	2	0.5	0	2
4	0.5	0	2	0.5	0	2
5	0	0.5	0	0.5	0.5	7
6	4	1.5	4.5	5	3.5	6.5
7*	2.5	5.5	4.5	1.5	3.5	4.5
8*	1	0.5	4	0.5	0	5
9	0	0	0	0	0	0
10*	3.5	4.5	2	1.5	1	2
11	-	-	-	-	-	-
12	1	4.5	3	1	0.5	3
13	1	0.5	4	0.5	2	5
14*	1.5	1.5	4	1	0	2
15*	1	3.5	5.5	0.5	0.5	3
16*	1.5	2	5.5	0.5	1	2
17*	2	1.5	3.5	1	1.5	1
18*	1	2	6	0.5	0.5	5
19*	1.5	2	2	0.5	0.5	3

Note: Negative Interactions = mean scores of the number of negative social interaction reported via the social interaction diary over a 3-day period during the baseline phase (pre-training) and after the training phase (post-training). Situations Avoided = mean scores of number of potentially negative social situations avoided (again via self-report diary) over the same 3-day periods, pre and post training. Emotional Response = mean scores of how upset or angry the participant felt immediately after their most negative interaction each day, on a scale of 0-7. Participant 11 had email issues and therefore was unable to receive/send any questionnaires. *Individuals for whom at least two of the social interaction diary items showed a reduction from assessment 3 to 4.

Quantitative data: Changes in Social Anxiety. Across participants, significant main effects of phase ($F(1,18)=11.68, p=.003, \eta_p^2=.39$) and time ($F(1,18)=5.70, p=.028, \eta_p^2=.24$) and their interaction ($F(1,18)=5.14, p=.036, \eta_p^2=.22$) emerged. Decomposing the interaction showed that the extent to which social anxiety scores differed across time varied with phase. Tests of simple main effects showed that SAS-A means were not significantly different between pre-baseline and pre-treatment assessments but instead decreased significantly between the post-baseline and post-training assessments ($F(1,18)=14.27, p=.001, \eta_p^2=.44$). Moreover, SAS-A means were not significantly different from pre-baseline to post-baseline,

but did significantly decrease pre-training to post-training ($F(1,18)=7.49, p=.014, \eta_p^2=.29$). Looking at the individual data, particularly social anxiety symptom scores at assessments 3 and 4 for, suggested some variability in symptom improvement; 68% of the 19 participants showed a reduction in symptoms across session assessments 3 and 4; although it is worth noting that the range in reported symptom reduction was large (-1 to -19; individuals who reported a reduction are marked with * in Table 3.4). A minority (26%) of participants showed an increase in symptoms (+2 to +6) and one participant reported no change.

Quantitative data: Changes in Social Interactions. Across participants, a significant reduction in the number of negative social interactions experienced from pre ($M=2.89, SD=2.30$) to post ($M=1.89, SD=2.17$) training ($t(17)=2.47, p=.024, d=.58$) was found. The number of social interactions avoided also significantly reduced from pre ($M=3.61, SD=3.36$) to post ($M=1.94, SD=2.18$) training ($t(17)=2.21, p=.041, d=.52$). A paired samples t-test on affect ratings showed a significant reduction in immediate emotional response pre ($M=6.63, SD=3.26$) to post ($M=4.38, SD=2.92$) training ($t(15)=2.45, p=.02, d=.61$). Data for individual participants showed that only 53% of the 18 participants with valid data showed a reduction on at least two of the items from the social diary assessments from pre to post-training.

Quantitative data: Changes in General Anxiety. There was a significant main effect of phase ($F(1,18)=24.77, p<.001, \eta_p^2=.58$) as well as a significant time-by-phase interaction ($F(1,18)=6.73, p=.018, \eta_p^2=.27$). Post hoc analyses revealed that SCARED means were not significantly different pre-baseline and pre-treatment assessments, but did significantly decrease from post-baseline and post-training assessments ($F(1,18)=22.19, p<.001, \eta_p^2=.55$). SCARED means were not significantly different pre-baseline and post-baseline assessments, however did significantly decrease from pre-training to post-training assessments ($F(1,18)=8.21, p=.01, \eta_p^2=.31$).

Quantitative data: Changes in Depression. The main effect of phase ($F(1,18)=6.05$, $p=.024$, $\eta_p^2=.25$) and the interaction between time and phase ($F(1,18)=10.51$, $p=.005$, $\eta_p^2=.37$) were significant. Tests of simple main effects for phase and time found that MFQ means were significantly decreased between post-baseline and post-training assessments ($F(1,18)=13.36$, $p<.002$, $\eta_p^2=.43$), but not between pre-baseline and pre-training assessments. For effects of time, there was a significant reduction between pre- and post-training assessments, ($F(1,18)=7.54$, $p=.013$, $\eta_p^2=.30$), but not between pre- and post-baseline assessments.

Quantitative data: Changes in Cognitive biases. Participant mean scores on the assessments of interpretation and attention biases are presented in Table 3.6.

Table. 3.6 Mean (Standard Deviation) of AIBT and Dot Probe Scores.

Time-point	Baseline Phase		Training Phase	
	Pre	Post	Pre	Post
Session	Assessment 1	Assessment 2	Assessment 3	Assessment 4
N	19	19	19	19
AIBT Bias Score	-6.37(11.16)	-3.95 (10.57)	-4.21 (9.72)	1.32 (9.28)
AIBT - Total positive ratings	13.16 (5.58)	16.42 (5.50)	16.95 (6.03)	19.42 (5.87)
AIBT - Total negative ratings	19.53 (6.03)	20.37 (5.61)	21.16 (4.94)	18.11 (5.84)
Dot Probe Bias Score – words (ms)	-18.1 (113.12)	44.3 (79)	26.3 (63.39)	5.4 (66.72)
RT - Neutral	678.6 (181.24)	614.2 (122.22)	591.4 (123.88)	525.5 (87.89)
RT - Threat	696.7 (259.73)	569.9 (77.74)	565.1 (98.14)	520.1 (71.1)
Dot Probe Bias Score – faces (ms)	11.9 (67.4)	21.7 (81.6)	22.1 (53.9)	15.2 (42.0)
RT - Neutral	634.1 (125.2)	558.5 (59.0)	567.0 (109.3)	514.0 (74.9)
RT - Threat	622.2 (112.6)	580.3 (117.1)	589.1 (104.6)	498.7 (60.3)

*N=18 for dot probe data due to exclusion of outlier.

Note: AIBT = Adolescent Interpretation Bias Task; RT = Reaction Time; ms = milliseconds

Interpretation bias. Main effects for both phase ($F(1,18) = 7.08, p = .016, \eta_p^2 = .28$) and time ($F(1,18) = 18.29, p < .001, \eta_p^2 = .50$) were statistically significant but not their interaction. Nonetheless, given the observed large decrease in bias score pre- to post-training, and given that our a priori predictions were that changes would happen during training phase, a post-hoc one-way ANOVA was run to explore main effects of time during each phase. There was no significant main effect of time during the baseline phase ($F(1,18) = 3.75, p = .069, \eta_p^2 = .17$), however there was a significant increase in bias score (more positive than negative interpretations) between pre- and post-training assessments ($F(1,18) = 14.25, p = .001, \eta_p^2 = .44$). Furthermore, there was significant increase between post-baseline and post-training assessments ($F(1,18) = 7.79, p = .012, \eta_p^2 = .30$), and no significant difference between pre-baseline and pre-training assessments.

Attention bias. Analysis of the neutral-threat (faces) dot probe data found no significant effects. The same analysis of the neutral-threat dot probe using words found neither of the main effects for phase or time reached statistical significance, however the interaction between time and phase was significant ($F(1,17) = 6.07, p = .025, \eta_p^2 = .26$). Post hoc analyses found that bias score means significantly differed only between post-baseline and post-training assessments ($F(1,17) = 4.8, p = .043, \eta_p^2 = .22$). No significant effects were found for neutral-positive dot probe bias scores using words. The same analysis of the neutral-positive dot probe using faces found main effects for both phase ($F(1,17) = 5.90, p = .026, \eta_p^2 = .26$) and time ($F(1,17) = 5.30, p < .034, \eta_p^2 = .24$) were statistically significant but not their interaction.

Quantitative data: Correlations between change in symptoms and change in biases.

Bivariate correlations showed that increased interpretation bias scores on the AIBT from pre- to post-training (i.e. an increased readiness to interpret ambiguous events less negatively) was

significantly associated with reductions in SAS-A scores pre- to post-training ($r = -.56$, $p = .012$). Correlations between change in attention bias scores, as measured by dot probe bias scores for selective attention toward threat (words) and change in symptom scores on the SAS-A, pre- to post-training, were not significant. There was also no significant correlation between change in symptom scores on the SAS-A and change in selective attention bias scores toward threat when using face stimuli.

3.4. Discussion

This case series explored the value of a combined-bias, multi-session CBM program, for adolescents with elevated social anxiety. While targeting both attention and interpretation biases for threat, new training modules targeting self-focused attention and internal attributions were included as well as a variety of training techniques that used both verbal and pictorial stimuli to enhance user-engagement. The data obtained suggest that it is viable to deliver this CBM program in a school in individual sessions with a trained researcher. Under experimental conditions, the program showed itself to be feasible in terms of its applicability and accessibility in a school setting: only 4 of the 23 participants withdrew from the study prior to completion, thus it appears to have a good acceptability from participants. Although not directly assessed, school teachers were largely supportive of this research and we had good recruitment rates amongst schools. It should be noted that participants were always accompanied by a researcher and some participants received several reminders of their appointment and needed supervision by a researcher in order to remain engaged in the training tasks. Some participants were fully engaged throughout the entire study without additional support from the researcher. This has implications for determining whether a CBM program such as the one used in this study, delivered in a school, is engaging enough for individuals to complete without supervision.

The significant reduction in symptoms on the SAS-A following eight sessions of CBM over 2-weeks, compared to no significant reduction in SAS-A scores following a 2-week baseline phase – and similar findings using a diary measure of daily social interactions – suggests that there is some potential in reducing social anxiety levels in adolescents reporting elevated symptoms. However, there are two caveats to this conclusion. First, although 13 participants showed changes on social anxiety symptoms, these varied between a decrease of 1 to 19, across the training phase, possibly suggesting that a few individuals with large changes drove the significant decreases. Also, only around 9 showed reductions across items on the social diary assessment. This suggests variability in how useful this training was for targeting social anxiety across individuals, reflected somewhat in the qualitative feedback too. Second, data from other outcome measures showed that these effects were not specific to social anxiety, and instead reductions in depressive and general anxiety symptoms were also observed. It is possible the observed decrease in socially-avoidant behaviour led to increased exposure to potentially rewarding social situations, thus having an impact on these general affective indices. However, as all of these measures were self-report, we cannot rule out the possibility that these broader symptoms changes indicate the presence of demand effects.

Also challenging for our findings of symptom improvement was mixed findings around changes in interpretation and attention bias. Although post-hoc analysis showed that interpretation bias scores did show a significant change pre- to post-training with no significant change pre to post baseline, the absence of a significant interaction effect between phase and time suggests that the degree of change was not significantly greater. However, individual scores show that for most participants the interpretation bias went in the intended direction, and several participants showed a greater jump from Assessment 3 to Assessment 4 than from Assessment 1 to Assessment 2. The feedback, on the whole, also points to several participants feeling the CBM-I tasks were beneficial. Finally, there was a significant association between this change in interpretative style and change in social anxiety

symptoms. It should be noted that, whilst there was a lack of significant correlation between initial baseline interpretation bias and SAS, the correlation reported was in the expected direction. With a larger sample size, we would expect this to reach significance. Furthermore, a weak correlation between initial interpretation bias and SAS may not be a prerequisite of a correlation between changes in these two variables, if the common factor explaining this correlation is the administration of a training tool designed to effect changes on both. Therefore, we tentatively suggest biased interpretations could provide a promising target for symptom improvement for some young people.

In contrast, we found no significant effects for attention bias change, or any correlation between change in attention bias to threat and change in symptoms. There was also a lack of significant correlation between cognitive biases and symptom measures at baseline. It may be that our current method for assessing attention bias is problematic. Previous research has shown the dot probe task has poor reliability, comprising internal consistency and test-retest reliability in children and adolescents (Brown et al., 2014; White et al., 2016)) and in adults (Van Bockstaele et al., 2017). Indeed, the current results display an extremely low test-retest reliability for attention bias $r = -0.01$), compared to the interpretation bias measure ($r = 0.88$). Some studies using eye-tracking have demonstrated that certain measures, such as dwell time across trials on socially threatening stimuli, are more reliable across time, but also more consistent in their associations with anxiety (Lazarov et al., 2016). More generally, others have argued that a visual search grid could be more effective than the dot probe as a tool for more reliably measuring and more effectively modifying attention processes that are linked to anxiety (Mogg & Bradley, 2016; Van Bockstaele et al., 2017). The development and application of potentially more stable and reliable measures like these are essential to better understand the nature and modification of attentional biases. Furthermore, as participant feedback suggests that the rigidity of the dot probe task may result in a lack of motivation and task engagement, incorporating extrinsic

motivators, such as real-time performance feedback (Bernstein & Zvielli, 2014) and using this real-time performance data to tailor the task to the individual's optimal rate of learning, (Schnyer et al., 2015) may increase task engagement and improve attention bias change.

While the training task was generally acceptable, the feedback collected provides more insights into further features that could improve effectiveness and engagement. Participant feedback suggests that as the goal of the CBM-I training portion became clearer, it gradually gave the participant an understanding of not needing to view social situations so negatively. It may be that incorporating explicit instructions to practice the target bias may enhance CBM efficiency (Macleod, 2009). This could be particularly true for the CBM-A tasks, as feedback suggests participants found these tasks 'boring' and 'un-engaging', partly due to not understanding why they were doing them. Feedback regarding task-specific elements of the CBM program suggests that, contrary to expectations, word-based social situations were in fact more successful in creating visual imagery than the picture-based scenarios. Several participants found the unfamiliar visual stimuli harder to engage and immerse than the word-based descriptions. Use of more personalised picture stimuli may be of greater use. This feedback is in line with recent research finding no difference in outcome when attempting to improve CBM-I effectiveness by incorporating visual imagery (de Voogd et al., 2017a). Whilst we have no way of quantitatively assessing whether this study benefited from multiple vs single sessions of training, the qualitative feedback suggests that after several sessions of CBM-I training some participants benefited from increased insight, that they could 'look at social situations less negatively'.

Whilst the symptom changes on social anxiety are encouraging, the data also provide several challenges. That this study was a preliminary case series with a small sample size, the appropriateness of significance-testing of statistical comparisons is questionable with different approaches taken in prior studies, (Abeles et al., 2009; Bechor et al., 2014; Blackwell & Holmes, 2010; Rozenman, Weersing, & Amir, 2011). However, we limited our

statistical tests to key measures that related to a priori expectations. Second, although there are advantages to carrying out a A-B case series in the same participants (self-matching means that any potential confounders such as socioeconomic status, genetic risk, state of health etc., are automatically controlled for), the absence of an active control group or condition means we are unable to attribute symptom change directly to cognitive training procedures (over a placebo effect). Furthermore, this program was presented to participants as a new psychological training program designed to target cognitive biases, which may have increased demand effects and expectancy biases (See MacLeod et al., 2009 for a more thorough discussion of this issue). Use of questions to reveal expectancy beliefs (Schmidt et al., 2009) may be beneficial for future studies in assessing the possibility of demand effects. Additionally, as all participants completed the baseline phase prior to training and our design did not include a control group, we are unable to fully account for natural fluctuations in anxiety across time. However, as a first-step, such case series is important as performing a cross-over case series design and a randomised controlled clinical trial may be premature, and not an optimal strategy for investing research and patient resources. Third, the lack of bias effects might be to do with mixed training, as none of the training tasks were completed for more than two sessions. Fourth, the design could have benefited from a follow-up time point, with the possibility that all consequences of CBM may take a longer time to become evident. Previous CBM research has found that emotional outcomes continue post-CBM completion (Schmidt et al., 2009). Finally, the generalisability of our findings was affected by the strong gender disparity in our sample: female pupils self-selecting into such studies have been a feature of school-based recruitment in many of our studies. As students were allowed to ‘opt out’ of the screening procedure, there was little we could do to change this. Despite these limitations, we find the study has provided some encouraging findings. The CBM program has demonstrated its potential as an easily accessible resource for adolescents

with elevated social anxiety. The next step will be to test these tasks in a larger sample with a comparison condition or group.

Chapter 4

4

Attention Bias Modification with Feedback (ABM-F): Evaluation of a new method to target attentional bias with real-time feedback

This chapter presents a newly developed attention bias modification training task incorporating feedback (ABM-F), aiming to boost task engagement and reduce attention biases thought to maintain anxiety in adolescents. One hundred and thirty-nine adolescents (16-18), selected for elevated anxiety, were randomly allocated to one of three ABM-F conditions for one session of training. The first training condition provided ‘Performance Feedback’, indicating average reaction time at the end of each training block on a positive visual search task. The second condition gave ‘Performance Dependent Feedback’, in which task difficulty was amended after each block of the positive search task, by altering stimulus display time for the upcoming block, based on performance. The third condition provided the same task with ‘No Feedback’. Results indicated no effect of ABM-F condition on attention bias change pre-to-post training on a visual search or dot probe measure. However, performance across the ABM-F task did decrease for the Performance Dependent Feedback group. Across all participants (collapsed across training groups), there was a pre-to-post training reduction in attention bias toward threat on the visual search task, but no transfer to the dot probe task. Differential changes on both attention bias measures pre to post training were found when comparing groups categorised by direction of attention bias at baseline (toward threat / away from threat / no bias). Finally, there were no effects on positive or negative mood. The findings suggest no differential effect of performance-related feedback on attention bias modification over one session but do provide implications for the influence of attention bias direction at baseline on modification outcome, and task performance in relation to feedback approach.

4.1 Introduction

In response to the high prevalence of anxiety cases emerging during adolescence (Beesdo et al., 2009; Ollendick et al., 2014; Polanczyk et al., 2015) and its detrimental long-term effects if left untreated, (Bruce et al., 2005), there has been an increasing focus on the development of readily accessible, adjunctive treatments to reduce anxiety symptoms at this vital period of development. With these factors in mind, one cognitive training task that has developed as a potentially viable treatment option is Attention Bias Modification (ABM) - a computer-based intervention that aims to ‘correct’ or modify attentional biases towards threat, thought to maintain symptoms amongst anxious individuals (MacLeod et al., 1986). Although there is data from systematic reviews and meta-analyses confirming the presence of attention biases amongst those with elevated anxiety in both adults (MacLeod & Clarke, 2015), and adolescents (Abend et al., 2018a; Dudeney et al., 2015; Klein et al., 2017; Puliafico & Kendall, 2006), modification of these biases has not consistently been associated with symptom reduction, or if present, these effects are weak (Cristea et al., 2015a). This has led to widespread efforts to identify task parameters or individual differences to enhance the modification of biases and subsequent symptom reduction (MacLeod & Clarke, 2015). Therefore, the goal of this chapter is to evaluate the effectiveness of a new ABM task variant, which aims to increase task engagement and subsequently produce greater bias modification effects. This chapter also aims to evaluate whether existing individual differences in attention bias pre-training affect responsiveness to this ABM approach.

In response to the mixed results from ABM, suggestions to improve training effects have often focused on the need for task improvements and adaptations in order to counteract the tedious nature of existing ABM tasks (Cristea et al, 2015b; MacLoed & Clarke, 2015; McNally, 2018; Mogg, Waters & Bradley, 2017). Indeed, participant feedback collected in chapter three, following a combination of dot probe and positive visual search training, serves to illustrate how the issue of task engagement and motivation may be hampering task

effectiveness. The majority of participants indicated that the rigidity and repetitive nature of the attention training tasks resulted in a lack of motivation and engagement. If participants are not actively engaged with the (necessarily repetitive) process, this is likely to have a detrimental effect on how efficiently the bias can be modified. In fact, it has been shown that increased rate of learning across ABM training correlates with improvement in symptoms in young people and adults but is more difficult to achieve in younger participants (Abend et al., 2018b; Bar-Haim et al., 2011). Therefore, task engagement may be particularly important for children and adolescents.

Research reviews showing more successful outcomes from laboratory-based studies than remote/internet-delivered studies (Cristea et al., 2015b; Linetzky et al., 2015; Mogg & Bradley, 2018; Mogg, Waters, & Bradley, 2017) suggest that when the individual is being monitored and/or encouraged to continue with the task they are more likely to engage with the training and see favourable outcomes. In turn, this suggests ABM tasks improving user engagement and motivation may allow for more effective autonomous use of ABM training and reduce the need for ‘supervision’ in order to obtain satisfactory outcomes. These issues leave us with the important question of ‘how can we ensure the latest adaptations of ABM programs limit distractions and consistently achieve maximum task engagement in young people?’.

4.1.1. Real-time feedback

One approach is to individualise the task based on the participant’s performance. A way to achieve this could be by the use of real-time feedback: using feedback of task performance could offer the opportunity to provide explicit information on progress to optimise learning through re-enforcement, or covertly tailor the task to the individual for optimal learning by continuously updating parameters based on performance. In fact, with many existing elements of ABM tasks not feasible to alter, feedback provides an option that

is easy to adapt to the individual and could have a significant effect on motivation. Real-time feedback has already been used in several other modalities to optimize task learning, such as the use of neurofeedback to improve the learning of emotion regulation strategies, discussed further in chapter five. Attention research has also recently started to incorporate extrinsic motivators, such as real-time feedback, to improve task performance: Bernstein and Zvielli (2014) provided computerized real-time feedback regarding the participants' allocation of attention (level of bias) at several time-points throughout a dot probe task. This resulted in a reduction in attentional bias to threat pre- to post-training. Using a different technology, Lazarov et al (2017a) extended a free-viewing eye-tracking task into a novel feedback task, in which the participant is prompted to return their gaze to a non-threatening stimulus by the pausing of a looped music track whenever their gaze dwells upon a threatening face. This approach resulted in successful attention bias modification and reduced social anxiety in adults, with adolescent trials currently underway. Utilising these ideas in order to adapt current attention training approaches may provide a more successful route to actively engage the individual and ameliorate attention biases. Whilst these neurocognitive and eye-tracking methods are promising, they also have the drawback of cost, availability and feasibility of using specialised equipment. It is currently not yet understood whether simple behavioural feedback, such as reaction-time feedback, could be just as effective in reducing biases and symptoms.

There is also evidence showing these real-time feedback methods can be utilised in a more covert manner, by updating task parameters continuously in order to individualise the intervention to the participant (Schyns et al., 2015). Schyns and colleagues used real-time feedback of activity in attentional brain networks to continually update task parameters of a visual search training task based on performance. Task difficulty was altered (by adding more distractors compared to target stimuli) in response to a performance change, as continuously assessed by brain activity. Therefore, it is possible that by monitoring performance and

adapting the task to the individual's differential rate of learning during training we could produce a more personalised and challenging experience that engages the individual more successfully and improves the effectiveness of ABM training. There is also data showing that presenting anxious participants with other emotional information, such as an upcoming speech, during the Stroop task reduces the interference effect (Mathews & Sebastian, 1993). This suggests that competing task demands, which presumably increase recruitment of voluntary attentional resources to goal-directed behaviour, can simultaneously reduce involuntary attention towards threatening stimuli, thus suppressing anxiety-linked attention biases. In fact, the increase in distraction (i.e. cognitive load) may actually improve training effectiveness. Clarke et al (2017) found that participants receiving ABM training under increased working memory load demonstrated significantly greater reduction in attentional bias compared to those receiving ABM training under no load. The authors suggest that recruitment of greater cognitive resources may have elicited (or even enhanced) attentional control and prompted greater sensitivity to the training contingency. Therefore, providing a more challenging task experience, of increasing task difficulty based on individual performance, may also improve training effectiveness through increased cognitive demands, but this has yet to be assessed.

4.1.2. Task selection

Task selection is also likely to be a key factor in training success. The extensive review of multi-session ABM studies carried out by Mogg, Waters, and Bradley (2017), concluded that threat-avoidance training (as carried out with a dot probe task) may not be the most effective method for reducing anxiety. They discovered that anxiety reduction is most strongly associated with positive visual search training; suggesting that tasks such as this, which recruit goal-directed cognitive-control processes to train against threat processing, as opposed to simply targeting one specific threat-orienting bias (as in the dot probe task), may

be more effective in reducing anxiety. Indeed, recent studies of anxious young people have reported promising (yet varying) results using positive visual search training with children and adolescents (de Voogd et al., 2014; de Voogd et al 2016; Waters et al., 2013; Waters et al., 2015), suggesting the positive visual search approach to attention training may provide a more promising tool for attention bias modification training, but requires optimisation. Thus, working with the idea that positive visual search training may present a favourable option for attention training, this study focused on whether improvements could be made in task engagement and learning efficiency on this task with the use of real-time feedback.

4.1.3. Pre-existing attention bias

A final factor to consider is the current uncertainty over whether pre-existing attention bias can influence the degree to which individuals respond to ABM protocols. Across studies, there is a mixed pattern of findings in regard to pre-existing attention biases; the meta-analysis in chapter two found eye-tracking tasks have demonstrated no difference in first fixations to threat in anxious versus non-anxious youth. Mogg, Waters, and Bradley (2017) reviewed 34 adult RCTs, and found that in most ABM studies anxious individuals showed no pre-existing bias toward threat. They pertinently point out that this remains a fundamental assumption of ABM training, with most studies training participants attention away from threat. Thus, ignoring individual differences in initial direction of attention bias may affect ABM outcome. There has been some investigation specifically into whether the initial bias direction affects change in attention bias pre to post-training: Fox et al (2015) investigated the effect of initial bias direction on outcome of ABM training for spider-phobic adults, finding that those who displayed an initial bias toward threat showed a greater change in attention bias following dot probe training. O'Toole and Dennis (2012) found similar results in non-anxious adults, with only initial bias toward threat predicting significant improvement in threat-bias. Thus, studies using adult participants with a dot probe task have found initial

bias direction to be an important factor in training outcome. However, this has been less readily investigated in younger participants, and with other ABM tasks. One study of anxious children did find a positive association between threat-bias pre-intervention and symptom reduction after positive visual search training (Waters et al., 2015), however, they did not evaluate the effect of initial bias on attention measures. Therefore, a logical extension to these findings is to investigate how the specific direction of initial bias may affect the training outcomes of positive visual search training, in adolescents. Theoretically one would expect those with an initial bias toward threat to be more suitable for dot probe ABM training, however, with positive visual search training seemingly more suitable for all anxious individuals, due to its proposed recruitment of several top-down cognitive-control functions (Mogg, Waters & Bradley, 2017), there may be an attentional and/or anxiolytic effect on individuals with and without an initial threat-bias.

4.1.4. Study aims

In light of the discussed evidence, this study proposes the incorporation of two feedback mechanisms into a positive visual search-based ABM training task, to produce a novel cognitive training task to target attentional biases in adolescents with heightened levels of anxiety. The first ABM-Feedback (ABM-F) task will employ performance-based feedback, in which the participant receives regular information regarding their performance (reaction time) on the task. The second ABM-F task will use performance-dependent feedback, in which task difficulty is regularly altered based upon the ongoing performance of the individual. The third condition will employ no-feedback, using a standard positive visual search task. To allow investigation of whether any training effect transfers to a different measure of attention, the dot probe task will be used in addition to Emotional Visual Search Task (EVST; de Voogd, Wiers, Prins, & Salemink, 2014) to assess attention bias pre- and post-training. Initial threat bias (toward threat / away from threat / no-bias) will also be

calculated and analyses will investigate its impact upon attention bias and mood changes pre- to post-training.

It is hypothesized that all ABM-F tasks will produce an improvement in attention bias on the EVST, and this will transfer to a reduction in attention bias toward threat on the dot probe tasks. Furthermore, it is predicted that those task conditions including feedback will result in greater attentional change than the no-feedback variant. However, due to a lack of prior research comparing these forms of feedback, we do not predict specific differences between the two feedback types. Based on prior research, we hypothesise that initial bias toward threat will make individuals more amenable to significant bias change, and therefore those displaying an initial bias toward threat will show a greater pre to post bias change in the desired direction than those who do not display this initial bias.

As secondary hypotheses, we expect task performance during the ABM-F training to be higher for those in the feedback conditions, due to greater task engagement. We also tentatively suggest, due to this greater engagement, there may be a greater decrease in negative mood and increase in positive mood following feedback training, compared to no-feedback training. Finally, it is notable that across studies of attention biases and youth anxiety, a variety of threatening faces have been used but with little consensus over whether one type of negative face yields a greater effect than another. An exploratory goal of this study was to compare whether angry or disgust faces yielded greater anxiety-linked attention biases and changes from attention bias modification. As no such differences emerged, these findings are included in appendix B.

4.2. Methods

4.2.1. Participants

Adolescents aged 16-18 years were recruited from secondary schools and sixth form colleges in London and King's College London University. Six hundred and eighty-nine individuals (92 male, 597 female) completed the pre-screening Revised Children's Anxiety and Depression Scale (RCADS; Chorpita, Ebesutani, & Spence, 2015). As our main interest was bias modification rather than specific effects on symptoms, and in the hope of recruiting as many participants as possible, it was decided to use a broader range of anxiety rather than a specific anxiety disorder, such as social anxiety. Using the recommend cut-off for borderline or clinical anxiety (Chorpita et al, 2015), 171 eligible students (142 females and 29 males) were invited to take part in the main study. 140 (114 females and 26 males) students agreed, with one of these participants dropping out shortly after commencing the testing session, due to illness, leaving 139 students who completed the entire study (114 females and 25 males). As all participants were over 16 years, they provided informed consent. Ethical approval for this protocol was granted by the Psychiatry, Nursing & Midwifery Research Ethics Subcommittee, King's College London (PMN-15/16-3263). Sample characteristics appear in Table 4.1.

4.2.2. Procedure

The study consisted of one testing session for each participant, lasting 45-60 minutes. Each participant was seen individually either in a quiet classroom at their school or a dedicated testing room at King' College London University, supervised by a researcher throughout. Prior to attendance each individual was assigned to one of three ABM-F conditions and within these, one of two threat-stimuli conditions, using random block allocation, with an equal number of participants assigned to each condition. Upon commencing the testing session, informed consent was collected along with a brief demographic form. The remaining session was completed using a laptop, starting with the pre-training questionnaire measures followed by the attention measures. Next, participants

completed the relevant ABM-F training they had been assigned. Participants then repeated the questionnaire and attention measures at post-training followed by a full debrief. Each participant received £5 for taking part.

4.2.3. Materials

Emotional face stimuli

Emotional face stimuli (neutral, happy, threat) were used from the NimStim faces set (NIMSTIM; Tottenham et al., 2009). Threat stimuli presented was either ‘Angry faces’ or ‘Disgust faces’. Participants viewing angry faces as the threat emotion, were presented with this threat emotion for all attention measures and training task. Likewise, those viewing disgust stimuli saw only disgust as the threatening emotion throughout the tasks. The same faces were used for the pre-training attention measures and the ABM-F training task, with different faces then used for the post-training measures of attention to control for any recognition effects.

ABM-F training task

Three ABM-F training conditions were applied: (i) Performance Feedback condition, (ii) Performance Dependent Feedback condition, and (iii) No-Feedback condition. In all conditions, participants completed a positive visual search attention training task consisting of 10 blocks, each containing 15 visual-search trials. In each trial, the search display was generated by randomly positioning a target item (happy face) amongst multiple distractor items (threat faces) within a 4 x 4 grid. The number of distractors varied from 1 to 15 across the block– with the trials presented in a random order. Each block was preceded by a fixation cross in the centre of the screen for 500ms. Participants were always instructed to click on the target face amongst the distractors as quickly as possible, regardless of condition. However, these conditions varied in the following ways:

(i) Performance Feedback condition

In this condition participants were presented with each trial until the correct response was made. When the target face was successfully clicked on with the mouse, the task continued to the next trial. Reaction Time (RT) data was recorded from each successful response and used to calculate the mean RT for each block of 15 trials. At the end of each block the mean RT was fed back to the participant in the form of a performance thermometer (see figure 4.1), which showed their current performance (RT) marked on bar, compared to their performance in the previous block (from block 2 onwards). This continued following each of the 10 blocks.

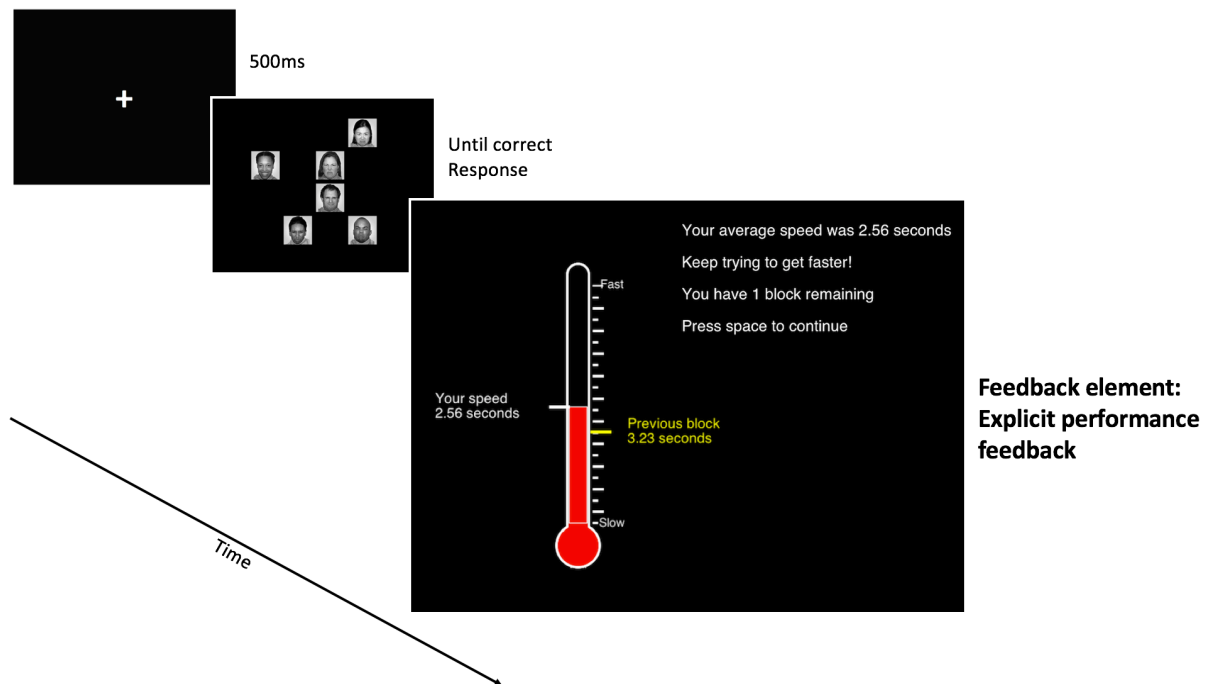


Figure 4.1. Sequence of stimuli presentation for the Performance Feedback condition

(ii) Performance Dependent Feedback condition

In this condition participants completed a positive visual search task with the same basic parameters and stimuli (fig. 4.2). However, during this condition feedback occurred through continuous alteration of task parameters – specifically stimulus presentation time. The display time was altered based upon performance to attempt to provide optimal conditions to

retain a level of difficulty that kept the participant engaged in the task and resulted in continuous improvement (speed of response). At the start of the task, the participant was simply instructed to select the target face amongst the distractors as quickly as possible. As per condition 1, the first block presented each trial until the correct selection was made, with these response times then used to calculate the mean RT for block 1. The second block used this mean RT as the display time for each trial, before the next trial commenced, regardless of response. All the remaining blocks from block 3 onwards used performance of the preceding block to calculate display time for the next block with the following rules:

- If participants successfully responded to 60% of trials in the block (i.e. selected the target face before the faces disappeared) *and* their mean RT was >5% faster than the preceding block, then the display time for each trial of the next block was reduced by 7.5%.
- If participants got 60% of trials correct but their mean RT was not >5% faster than the preceding block, the display time remained the same for each trial of the next block.
- If they did not successfully respond to at least 60% of trials in the block, then display time for each trial of the next block was increased by 7.5%.

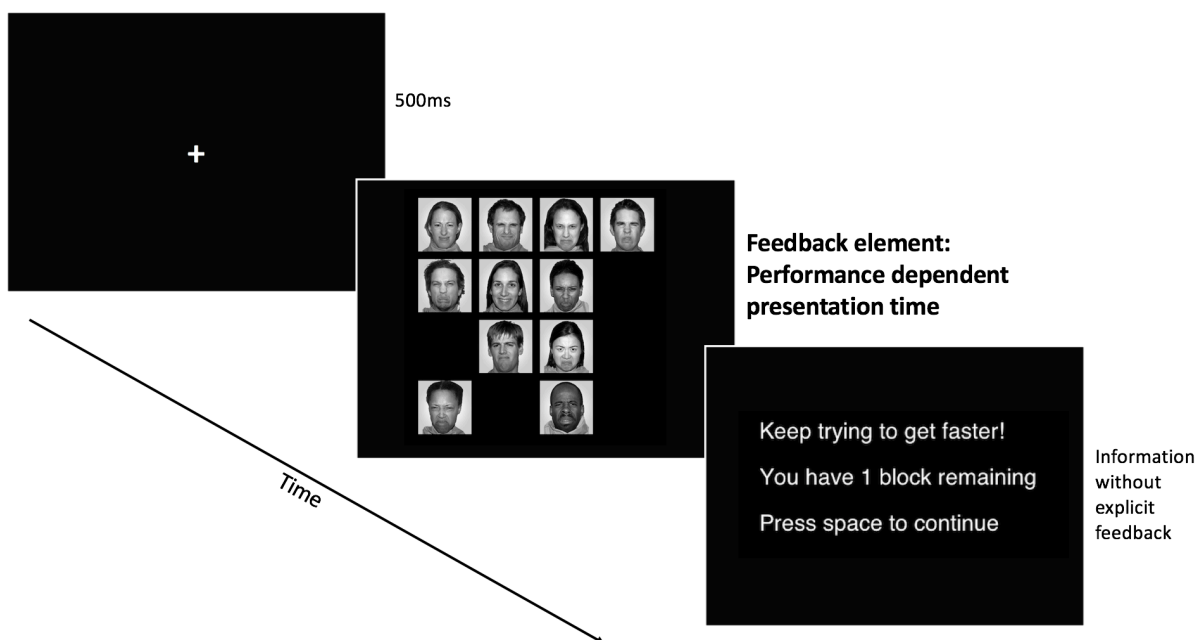


Figure 4.2. Sequence of stimuli presentation for the Performance Dependent Feedback condition

(iii) No-Feedback condition

This condition mimicked condition 1, with each trial presented until the correct response was made, across all blocks. However, in this case, no feedback was given at the end of each block and no alteration to task parameters was made based upon performance. A message of encouragement and information as to how many blocks were remaining, was presented after each block, as for all conditions.

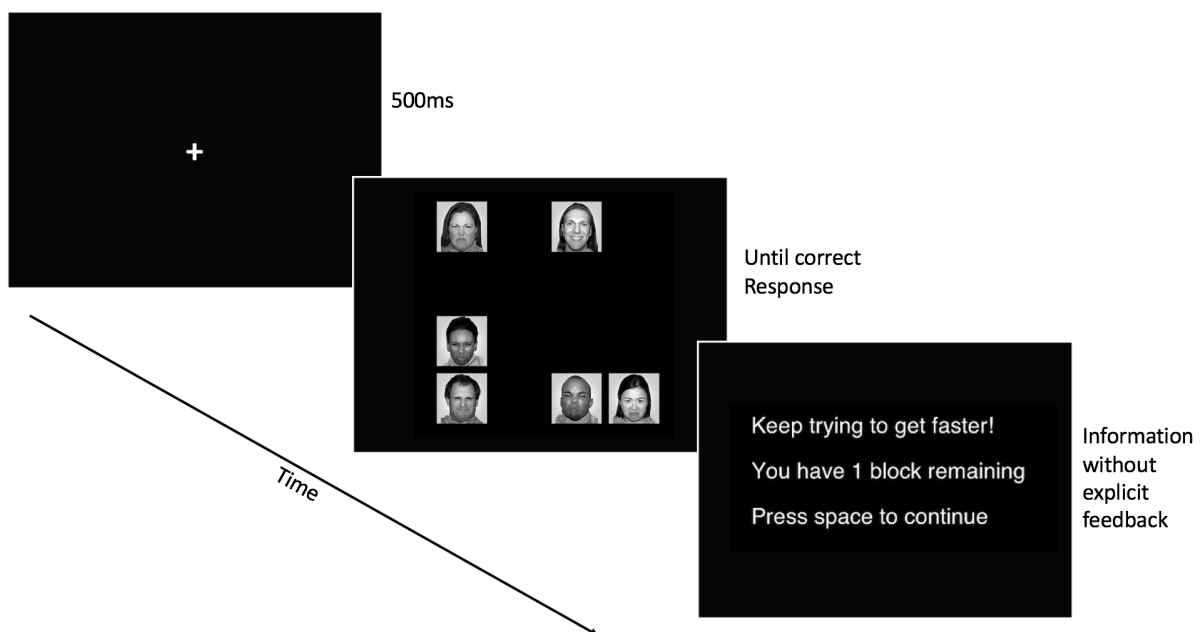


Figure 4.3. Sequence of stimuli presentation for the No Feedback condition

Correct response times were recorded for each participant throughout the task, and mean RTs for each block were computed. For condition 2, in order to take into account that RT would be largely influenced by the limited display time, we also included number of errors (classified by the number of trials where the stimuli disappeared before correct response) in our computation, in order to create a new “Inverse Efficiency Score” (IES; Bruyer & Brysbaert, 2011; Townsend & Ashby, 1978; Vandierendonck, 2017). The IES is calculated as $IES = RT / (1 - PE)$, where RT is the participant’s mean (correct) RT of the block, and PE is the participant’s proportion of errors in that block (Townsend & Ashby, 1978). The IES can

be considered as the RT corrected for the amount of errors committed. For each condition we calculated mean scores for Early blocks (2-4), Mid blocks (5-7) and Late blocks (8-10) to allow for easier comparison of performance across the task.

Attention Measures (all conducted pre and post-training)

Dot probe task

Participants viewed 80 trials during each training session, preceded by 8 practice trials. Of these 32 were Threat-Neutral (16 probe-behind-threat, 16 probe-behind-neutral), 32 were Threat-Happy (16 probe-behind-threat, 16 probe-behind-happy), and 16 were neutral-Neutral ‘filler’ trials (interspersed to reduce chances of habituation to the expressions). Thus, the probe appeared with equal probability behind each type of stimuli. We supplemented threat-neutral pairings with threat-positive pairings, as this provided a pairing more commensurate with the training task. Eight female and eight male faces were used. Each face pairing used the same actor. Each face pairing was shown four times for Threat-Happy and Threat-Neutral trials and twice for Neutral-Neutral trials. Each face photograph subtended 45mm in width and 34mm in height. The face photographs were presented with equal distance to the left and right of the fixation cross, with a distance of 14mm between them. Each trial began with the presentation of a fixation display for 500ms (white cross 1*1 cm at the centre of the screen), on which the participants were requested to focus their gaze. The fixation display was followed by a face pair display for 500ms, immediately followed by the target probe (“p” or “q”). Participants were required to locate the probe position and determine which symbol appeared by pressing one of the two pre-specified keys on the keyboard. The target remained on the screen until the participant responded.

Raw reaction time data for each participant was analysed and trials with a response time <150 ms or >3 standard deviations above the participant’s mean were eliminated from

further analyses, as were trials with incorrect responses, resulting in removal of 5.7% of all pre- and post-training trials. Participants who made incorrect or outlying responses on greater than 25% of trials were excluded from subsequent analyses (This resulted in 7 participants being removed from analysis). Following this, an attentional bias score was computed for each trial type (Bias Score = ProbeNeutral – ProbeThreat; or ProbeHappy – ProbeThreat). Positive bias score values indicate a bias towards Threat (vigilance bias) and negative values indicate a bias away from the Threat (avoidance bias). Participants with an extreme bias score (± 3 standard deviations from the overall group mean) were excluded, resulting in the exclusion of 5 participants' data from the dot probe analyses.

EVST (pre and post ABM-F training)

As per the ABM-F training task, a 4 x 4 matrix of 16 faces was presented, in which the participant had to search for the target face amongst the distractors. During this task the grid always contained 1 target face and 15 distractors. Participants were presented with one block of 32 trials with a target face displaying a happy emotion amongst distractor faces displaying threat (angry/disgust) emotion, and one block of 32 trials in which the target face displayed a threat (angry/disgust) emotion amongst distractor faces displaying a happy emotion. Distractor Faces were randomly positioned in each trial, with the target face located in different positions within the matrix an equal number of times. Block order was counterbalanced across participants. Each grid remained on the screen until a successful response, and Mean RTs were calculated for each block.

Outliers and errors were calculated in the same way as for the dot probe tasks, resulting in removal of 6.6% of all pre and post trials. Data from 4 participants were removed from EVST analyses due to incorrect or outlying responses on greater than 25% of trials. An EVST bias score was calculated by subtracting mean RT when searching for threat emotion from mean RT when searching for the happy emotion. Therefore, positive bias scores

indicate faster (vigilance) detection of threat. Participants with an extreme bias score (± 3 standard deviations from the overall group mean) were excluded, resulting in the exclusion of 1 participant's data from the EVST analyses. Furthermore, due to a technical fault, data for the first 13 participants was not recorded on the EVST (pre or post).

Initial bias calculation

In order to classify direction of initial bias for the EVST we used thresholds of 250ms either side of zero as criterion for "bias direction". A bias score of $> 250\text{ms}$ was classified as "Bias Toward Threat", and $< -250\text{ms}$ was classified as "Bias Away from Threat". Those scores falling between these values were classified as "No Bias". These directional indices were also calculated for the dot probe measures. In this instance, due to the differences in task action, thresholds of 25ms either side of zero were used as the criterion. This was based upon by Zvielli, Bernstein, and Koster (2014) and Fox et al., (2015). Therefore, for the dot probe tasks, a bias score of $> 25\text{ms}$ was classified as "Bias Toward Threat", and $< -25\text{ms}$ was classified as "Bias Away from Threat". Those scores falling between these values were classified as "No Bias".

Questionnaire measures

The Revised Children's Anxiety and Depression Scale – Pre and post training (RCADS; Chorpita, et al., 2015) – short version

This questionnaire contains 25-items that measure the frequency of various symptoms of anxiety and depression. SPSS syntax, provided by the scale creators, was used to produce a total anxiety score, which was then transformed into a t-score to account for age and gender differences. The t-score could also be assessed against pre-defined cut-offs for borderline and clinical levels of anxiety (65 and 70, respectively) for initial screening purposes. For the present study, internal consistency pre-training was $\alpha = 0.82$, and post-training $\alpha = 0.84$.

VAS – Pre and post training (Visual Analogue Scale)

This scale was used to measure mood along 11 dimensions: cheerful, gloomy, happy, sad, calm, nervous, anxious, worried, upset, miserable and energetic. Participants were asked to rate their mood by clicking the relevant place on a line marked from 0 to 100. E.g. “From 0 – 100, how nervous do you feel right now?”. A mean score was calculated for items combined into either a positive dimension or negative dimension, pre and post-training. For the present study, internal consistency for positive dimensions pre-training was $\alpha = 0.73$, and post-training $\alpha = 0.75$. Internal consistency for negative dimensions pre-training was $\alpha = 0.85$, and post-training $\alpha = 0.91$.

4.2.4. Statistical Analysis

Effect of ABM-F group and initial bias direction on attention measures: To test the hypotheses that the impact of a single session of ABM-F on EVST bias score would differ by type of feedback and initial bias direction, we assessed main and interaction effects from a 2x3x3 mixed ANOVA, with Time (pre-training EVST bias score, post-training EVST bias score) as the within subjects factor, and Group (Performance Feedback, Performance Dependent Feedback, No Feedback) and Bias Direction (Away from threat, Towards threat, No bias) as the between-subjects variables. To investigate whether any difference would transfer to an attention measure less similar to the training task, we conducted the same 2x3x3 mixed ANOVA, firstly with dot probe bias score (Happy-Threat) as the dependent variable, and then with dot probe bias score (Neutral-Threat) as the dependent variable.

Effect of ABM-F group on training performance: Due to the difference in performance measure for the performance dependent feedback condition we were unable to directly compare performance across groups, as this would be comparing a paradigm where RT is bound to change (due to the nature of the task conditions) with two conditions in which the

display time is uniform. Therefore, three separate one-way repeated measures ANOVAs were run to test changes in performance within each feedback group, across early, mid and late blocks. ***Effect of ABM-F group and initial bias direction on mood:*** Finally, to investigate whether training condition and initial bias direction had a differential effect on mood, measured by the VAS, we assessed main and interaction effects from two 2x3x3 mixed ANOVAs, with Time (pre-training VAS score, post-training VAS score) as the within subjects factor, and Group (Performance Feedback, Performance Dependent Feedback, No Feedback) and Bias Direction (Away from threat, Towards threat, No bias) as the between-subjects variables. Separate ANOVAs were conducted for positive and negative dimensions.

4.3. Results

Table 4.1. Sample Characteristics and Mean (Standard Deviation) of questionnaire and attention measures, pre and post-training.

		Mean (SD) Pre-training	Mean (SD) Post-training
<i>All</i> <i>N = 139</i>	Age (years)	16.75 (0.83)	---
	Percentage Male	17.99%	---
	RCADS Anxiety t-score	72.45 (10.10)	---
	VAS Positive	36.33 (15.12)	36.42 (15.35)
	VAS Negative	45.73 (18.27)	44.41 (21.13)
	EVST	55.6 (789.48)	-277.6 (649.65)
	Dot probe (Happy-Threat)	-3.7 (49.37)	2.6 (38.6)
	Dot probe (Neutral- Threat)	-4 (56.35)	-1.4 (46.24)
<i>Performance</i> <i>Feedback</i> <i>Group</i> <i>N = 48</i>	Age (years)	16.91 (0.87)	---
	Percentage Male	20.80%	---
	RCADS Anxiety t-score	72.67 (10.97)	---
	VAS Positive	35.88 (16.54)	37.19 (17.46)

	VAS Negative	45.90 (20.162)	44.78 (22.16)
	EVST	101.4 (779)	-232.2 (636.13)
	Dot probe (Happy-Threat)	-16.3 (59.42)	10.4 (32.96)
	Dot probe (Neutral- Threat)	-3.8 (60.01)	-5.7 (48.97)
<i>Performance</i>	Age (years)	16.56 (0.82)	---
<i>Dependent</i>	Percentage Male	17.80%	---
<i>Feedback</i>	RCADS Anxiety t-score	71.68 (9.47)	---
<i>Group</i>			
<i>N = 45</i>	VAS Positive	36.36 (14.36)	34.89 (14.21)
	VAS Negative	45.82 (15.82)	45.71 (19.60)
	EVST	-110 (801.11)	-318.8 (820.29)
	Dot probe (Happy-Threat)	4.9 (41.13)	0 (36.14)
	Dot probe (Neutral- Threat)	-7.4 (34.72)	0 (39.23)
<i>No Feedback</i>	Age (years)	16.77 (0.77)	---
<i>Group</i>	Percentage Male	15.20%	---
<i>N = 46</i>	RCADS Anxiety t-score	72.96 (9.92)	---
	VAS Positive	36.76 (14.65)	37.11 (14.28)
	VAS Negative	45.46 (18.85)	42.8 (21.81)
	EVST	167.4 (132.51)	-283.9 (620.22)
	Dot probe (Happy-Threat)	1.7 (13.79)	-3.2 (39.48)
	Dot probe (Neutral- Threat)	-0.8 (14.12)	2 (49.4)

Note: RCADS = Revised Children's Anxiety and Depression Scale; VAS = Visual Analogue Scale. ABM-F training groups were similar in terms of gender distribution, $\chi^2(2)=0.50$, $p=.78$, age, and baseline RCADS scores, all $F_s < 2.09$, all $p_s > .13$. Descriptives for all attention measures by initial bias and training condition can be found in appendix C.

4.3.1. Effect of ABM-F group and initial bias direction on attention measures²

EVST

A 2x3x3 mixed ANOVA, with Time as the within subjects factor, and Feedback Group and Bias Direction as the between-subjects variables, showed a significant main effect of Time, $F(1, 112) = 22.88, p < .001, \eta^2 = .17$. The mean EVST bias score went from positive pre-training ($M = 55.6, SD = 789.48$) to negative post-training ($M = -277.6, SD = 649.65$). As a positive score indicates a bias toward threat, this result indicates a change in the desired direction - a reduction in attention bias toward threat pre to post-training. There was a significant main effect of Bias Direction, $F(2, 112) = 103.96, p < .001, \eta^2 = .65$, but no significant main effect of Group, $F(2, 112) = .68, p = .51, \eta^2 = .01$, and no significant three-way interaction between Time x Group x Bias Direction, $F(4, 112) = 0.22, p = .93, \eta^2 = .01$. There was no significant interaction for Time x Group, $F(2, 112) = .42, p = .66, \eta^2 = .01$, but there was a significant interaction for Time x Bias Direction, $F(2, 112) = 21.61, p < .001, \eta^2 = .28$. Decomposing this interaction, shows that the extent to which bias scores differed across time varied by initial bias direction. Tests of simple main effects showed that mean bias scores were not significantly different between pre ($M = -764.5, SD = 430.9$) and post-training ($M = -593.3, SD = 582.7$) for individuals displaying an initial bias away from threat, $F(1, 42) = 2.21, p = .145, \eta^2 = .05$. However, bias scores did significantly change in the

² As an alternative to categorising participants by initial bias direction, we also investigated initial bias direction as a continuous predictor of change in attention bias. This was investigated by creating change scores (post minus pre) for each attention measure, which were each entered into a separate simple linear regression as the dependent variable, with initial bias score (for the corresponding measure) as the predictor variable. For EVST, the model was significant ($R^2 = 0.46, F(1, 119) = 103.09, p < .001$). It was found that initial EVST bias score significantly predicted change in EVST ($\beta = -0.72, p < .001$). For dot probe (neutral-threat), the model was significant ($R^2 = 60.4, F(1, 125) = 191.74, p < .001$). Dot probe (neutral-threat) score significantly predicted change in attention bias on the dot probe (neutral-threat) measure ($\beta_1 = -1.02, p < .001$). For dot probe (happy-threat), the model was significant ($R^2 = 60.1, F(1, 125) = 188.27, p < .001$). Dot probe (happy-threat) score significantly predicted change in attention bias on the dot probe (happy-threat) measure ($\beta_1 = -0.96, p < .001$). Therefore, for each attention measure it appears greater attention bias toward threat pre-training predicts a more negative change in bias score (i.e. a reduced attention bias toward threat) pre-to-post ABM-F training.

‘trained’ direction between pre ($M = 871.3$, $SD = 437.02$) and post-training ($M = 3.0$, $SD = 607.98$) for individuals displaying an initial bias toward threat $F(1, 43) = 58.42$, $p < .001$, $\eta^2 = .58$. There was also a significant pre ($M = 37.2$, $SD = 132.5$) to post-training ($M = -241.6$, $SD = 620.2$) change for individuals displaying no bias, $F(1, 33) = 7.54$, $p = .010$, $\eta^2 = .19$. This was also in the ‘trained’ direction.

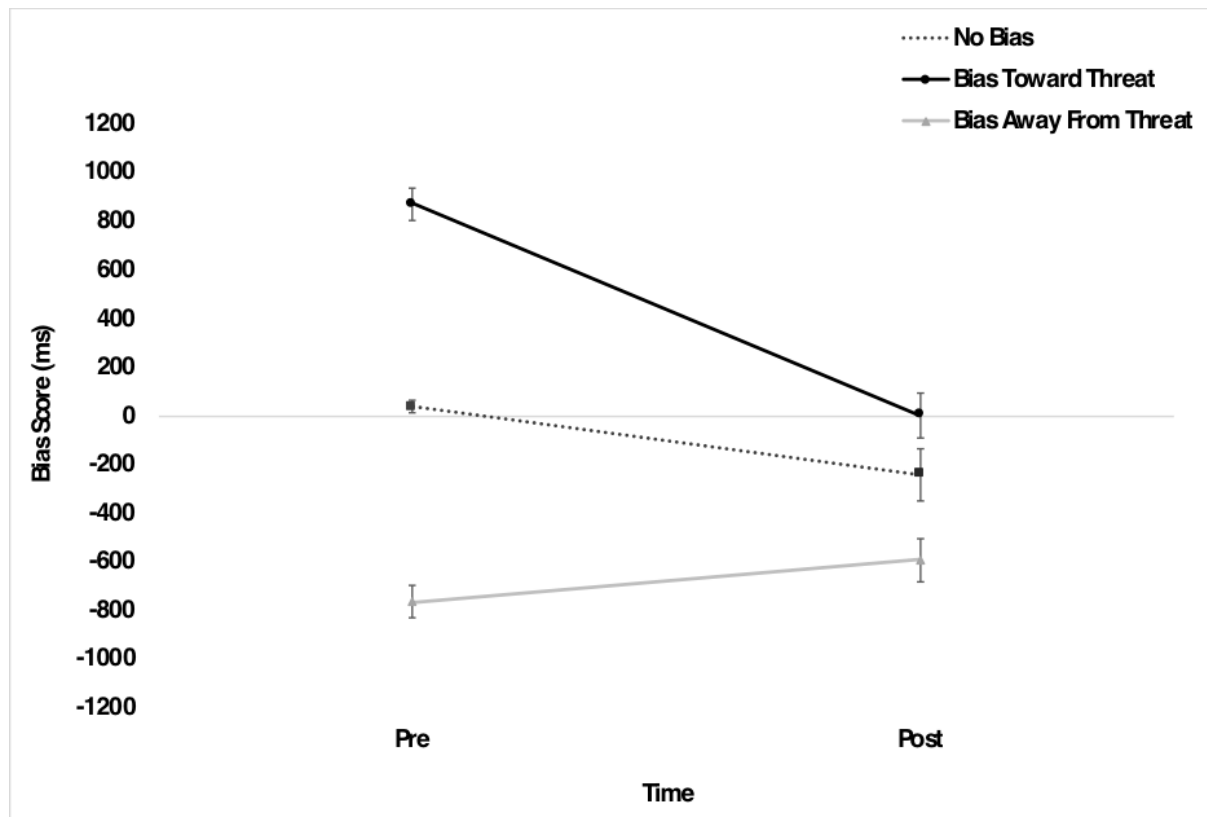


Figure 4.4. Mean EVST bias scores (with standard error bars) as a function of time-point and initial bias direction.

Dot probe (Happy-Threat)

A 2x3x3 mixed ANOVA showed a significant main effect of Bias Direction, $F(2, 118) = 46.79$, $p < .001$, $\eta^2 = 0.44$, but not of Time, $F(1, 118) = .001$, $p = .96$, $\eta^2 = .00$, or Group, $F(2, 121) = 0.39$, $p = .68$, $\eta^2 = 0.01$, and no significant interaction between the three, $F(4, 118) = 1.89$, $p = .12$, $\eta^2 = 0.06$. There was no significant Time x Group interaction, $F(2, 118) = 2.42$, $p = .09$, $\eta^2 = 0.04$, but there was a significant Time x Bias Direction interaction, $F(2, 118) = 43.00$, $p < .001$, $\eta^2 = 0.42$, showing that the extent to which dot probe bias scores

differed across time varied by initial bias direction. Tests of simple main effects showed that bias scores were not significantly different between pre ($M = 0.60$, $SD = 13.79$) and post-training ($M = 3.4$, $SD = 39.2$) for individuals displaying no bias, $F(1, 65) = 0.54$, $p = .47$, $\eta^2 = .01$. However, they did significantly decrease between pre ($M = 60.10$, $SD = 34.54$) and post ($M = 3.30$, $SD = 44.38$) training for individuals displaying an initial bias toward threat $F(1, 25) = 27.31$, $p < .001$, $\eta^2 = .52$, and there was significant pre ($M = -59.10$, $SD = 38.57$) to post ($M = -1.0$, $SD = 32.75$) training increase for individuals displaying an initial bias away from threat, $F(1, 34) = 46.95$, $p < .001$, $\eta^2 = .58$.

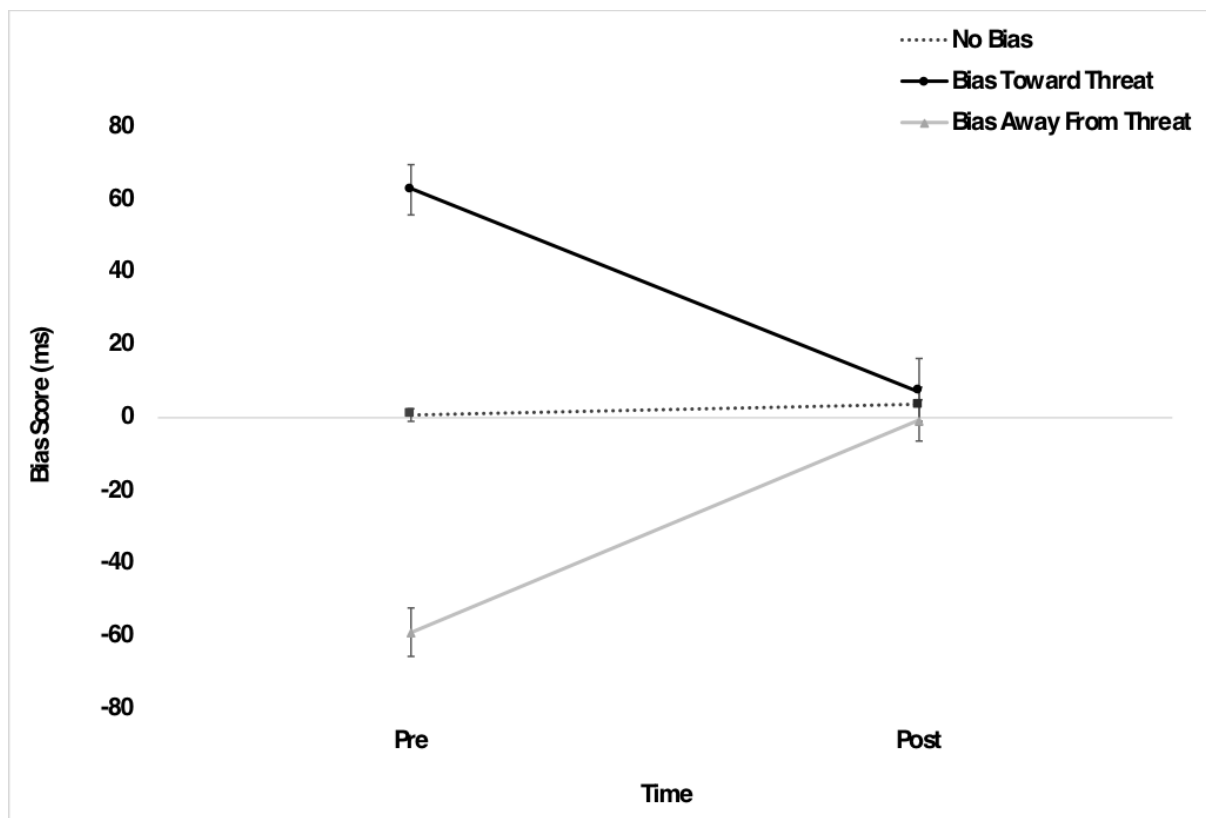


Figure 4.5. Mean (Happy-Threat) dot probe bias scores (with standard error bars) as a function of time-point and initial bias direction.

Dot probe (Neutral- Threat)

A 2x3x3 mixed ANOVA showed no significant main effect of Time, $F(1, 118) = 0.01$, $p = .94$, $\eta^2 = 0.00$, or Group, $F(2, 118) = 0.11$, $p = .90$, $\eta^2 = 0.00$, but there was a

significant main effect of Bias Direction, $F(2, 118) = 49.55$, $p < .001$, $\eta^2 = 0.46$. There was no significant Time x Group x Bias Direction interaction, $F(4, 118) = 1.86$, $p = .13$, $\eta^2 = .06$, or Time x Group interaction, $F(2, 118) = 0.39$, $p = .680$, $\eta^2 = 0.01$, but there was a significant interaction for Time x Bias Direction, $F(2, 118) = 29.75$, $p < .001$, $\eta^2 = 0.34$. Decomposing this interaction, shows that the extent to which dot probe bias scores differed across time varied by initial bias direction. Tests of simple main effects showed that bias scores were not significantly different between pre ($M = -0.90$ ms, $SD = 14.12$) and post-training ($M = -8.70$, $SD = 49.40$) for individuals displaying no bias, $F(1, 56) = 1.32$, $p = .256$, $\eta^2 = .02$. However, there was a significant decrease in bias score between pre ($M = 62.80$, $SD = 39.97$) and post ($M = 11.40$, $SD = 44.78$) training for individuals displaying an initial bias toward threat $F(1, 30) = 17.25$, $p < .001$, $\eta^2 = .37$, and a significant pre ($M = -61.50$, $SD = 43.83$) to post ($M = -0.80$, $SD = 41.77$) training increase in bias scores for individuals displaying an initial bias away from threat, $F(1, 38) = 33.27$, $p < .001$, $\eta^2 = .47$.

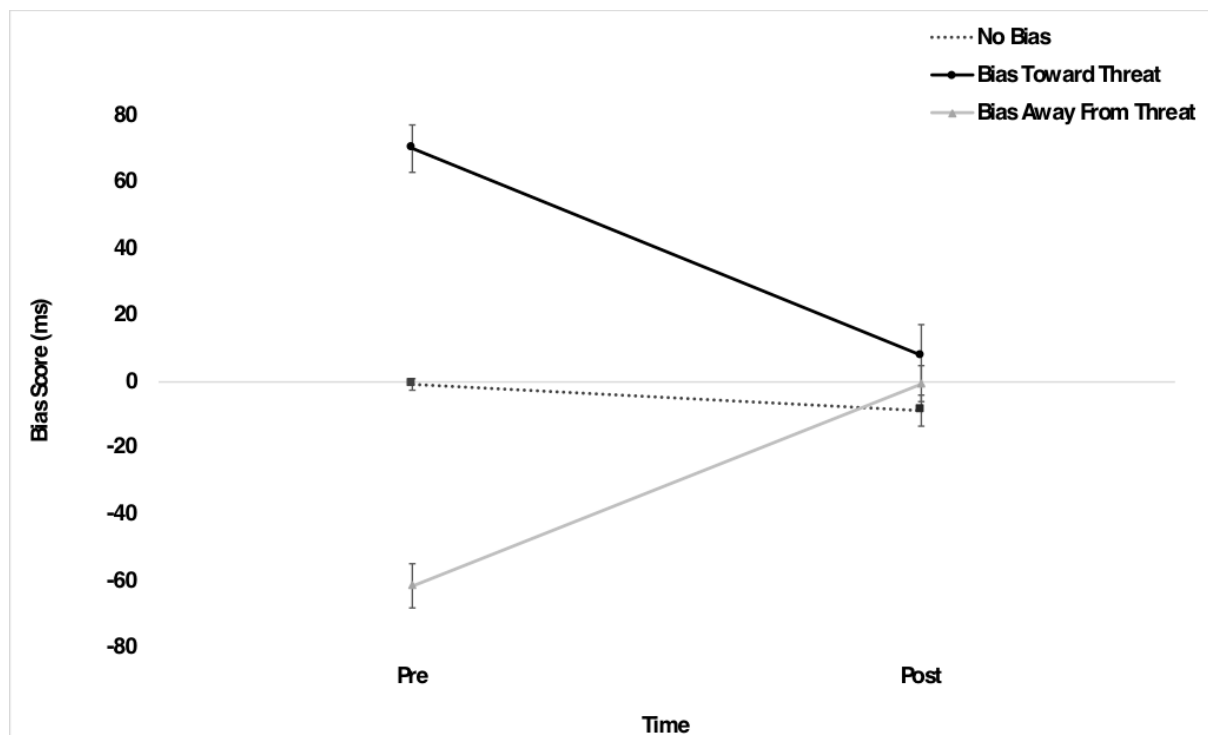


Figure 4.6. Mean (Neutral-Threat) dot probe bias scores (with standard error bars) as a function of time-point and initial bias direction.

4.3.2. Effect of ABM-F group on training performance

A repeated measures ANOVA for the performance feedback group showed that RT did not differ significantly across early, mid or late blocks, $F(2, 94) = 1.29$, $p = .281$, $\eta^2 = 0.03$. Likewise, the ANOVA for the no-feedback group showed no significant change in RTs across blocks, $F(2, 84) = 1.56$, $p = .21$, $\eta^2 = 0.04$. However, there was a significant effect of time for the performance dependent feedback group, $F(2, 88) = 8.04$, $p = .001$, $\eta^2 = 0.16$. Post hoc tests using Bonferroni correction revealed a significant difference between block one and two ($M=2.57$, $SD = 0.44$ vs $M= 2.70$, $SD= 0.44$, $p = .037$), and between block one and three ($M=2.57$, $SD = 0.44$ vs $M=2.81$, $SD = 0.45$, $p = .001$), but not between blocks two and three ($M= 2.70$, $SD= 0.44$ vs $M=2.81$, $SD = 0.45$, $p = .296$). Graphs illustrating performance in each training condition can be found in appendix D.

4.3.3. Effect of ABM-F group and initial bias on state mood

Using negative mood as the dependent variable, the $2 \times 3 \times 3$ mixed ANOVA, showed no significant main effect of Time, $F(1, 113) = 1.03$, $p = .31$, $\eta^2 = .01$, or Group, $F(2, 113) = .23$, $p = .79$, $\eta^2 = .00$, or Bias Direction, $F(1, 113) = 2.76$, $p = .07$, $\eta^2 = .00$. There were no interactions, (all $p > .26$). Using positive mood as the dependent variable, there was no significant main effect of Time, $F(1, 113) = .06$, $p = .80$, $\eta^2 = .00$, or Group, $F(2, 113) = .01$, $p = .99$, $\eta^2 = .00$, or Bias Direction, $F(1, 113) = 2.09$, $p = .13$, $\eta^2 = .04$. There were no interactions, (all $p > .56$).

4.4. Discussion

This study explored the effectiveness of incorporating different types of performance feedback into a positive visual search task aiming to modify attention biases in adolescents with elevated anxiety. The study also aimed to understand how the direction of initial attention biases would affect task effectiveness and performance, and whether any attention

bias changes would transfer between attention measures. When ignoring ABM-F group allocation and initial bias direction, the data obtained show a single session of positive visual search training resulted in a significant decrease in attention bias toward threat, measured by the EVST— a finding that did not generalise to dot probe measures. Feedback group allocation had no effect on bias modification effectiveness. Further differences in bias modification direction and magnitude did emerge when initial bias direction was taken into account. Training performance across the task showed significant change (in terms of response times) in only the performance dependent feedback group.

4.4.1. Feedback as a modification “booster”

ABM training did have an overall modification effect on the EVST measure, however the presence of either type of performance feedback did not alter task effectiveness compared to no feedback. Furthermore, the overall finding of bias modification did not generalise to the dot probe measures. It is possible the lab-based nature of this study may have restricted the emergence of feedback group differences. As discussed previously, results from ABM studies performed in laboratories have provided more consistent bias change than ABM taking place remotely (for example internet-delivered ABM). One reason put forward for this disparity is the lack of user engagement when performing the task without supervision. Therefore, these user engagement differences may disappear when in the laboratory, where there is very little distraction and the presence of a researcher. It is possible differences in user engagement (and thus task effectiveness) may be more exaggerated outside the laboratory and the use of engagement boosting methods (such as ABM-F) in these environments could produce significant differences in task outcome. Future research to see how these feedback conditions translate to remote ABM, where user engagement may be more variable, could provide interesting results. Furthermore, the current results don't provide any indication as to what effect feedback might have over longer time periods. It may be that over several sessions we

could see a more pronounced difference between feedback groups in performance and modification, as multiple sessions may be required to consolidate learning (Abend, Pine, Fox, & Bar-Haim, 2014).

4.4.2. Effects of initial attention bias

Whilst overall changes in mean bias score did not generalise to either dot probe measure, interesting findings emerge when initial bias direction is taken into account. When classifying participants by directionality of initial bias, and looking at the results irrespective of feedback group, a consistent pattern of effects emerges across dot probe measures. Namely, biases in either direction gravitate toward zero following training. However, those with no-bias at baseline, show no significant change pre to post training. The EVST shows a slightly different pattern of results when taking initial bias into account –as with the dot probe tasks, those with an initial bias toward threat show a significant change in the ‘trained’ direction. However, there is also a modest change in this direction for those with no bias. Those showing an initial avoidance bias on this measure do not demonstrate a significant change in any direction. These findings raise several points for discussion.

Firstly, the results demonstrate that when initial bias is taken into account bias modification effects show a similar pattern across dot probe measures, and that those with an initial bias toward threat show a significant reduction in this bias across all attention measures. However, more unexpectedly, those with an initial avoidance bias also show a change in bias, though moving away from the ‘trained’ direction. This pattern of results raises a strong possibility of regression to the mean. In fact, similar results were also observed by Fox et al (2015), who trained and measured spider phobic individuals with a dot probe task. Unlike Fox et al (2015), we also see this pattern of changes on a different attention task to that used during the training element. Therefore, an alternative explanation may be that the positive visual search task trains several attentional processes leading to

modification of existing attention bias regardless of direction: as suggested by Mogg and Bradley (2018), if cognitive processes, such as top-down cognitive control, play a significant role in attention biases then it is likely that a form of cognitive training which more broadly targets these processes will have a more consistent effect on existing attention biases in all participants. Therefore, it could tentatively be suggested that positive search training prompts improvements in flexible deployment of attention and enhances approach motivation, thus offsetting avoidant tendencies and impacting upon biased threat orienting biases in both directions (Waters et al., 2016). However, avoidance bias did not significantly change on the EVST (possibly due to the positive search training being identical in action to the ESVT measure), and it is difficult to explain why those with no bias at baseline on the dot probe task do not show any change following training. Therefore, this leaves regression to the mean as a realistic explanation, though certainly warranting further investigation.

The considerable variation in bias direction (and prevalence of no bias) at baseline supports assertions that bias toward threat may not be a stable characteristic of anxiety in adolescents (Wieckowski et al., 2018). Due to developmental differences, there may be particularly strong variation in this age group (Somerville, Jones, & Casey, 2010) - it may be the case that in some adolescents the bias is particularly unstable and not yet matured (Hankin et al., 2009). Alternatively, it may be the case that attention bias to threat only characterises a certain sub-set of anxious individuals. These findings are relevant for other studies of ABM, where variability in initial bias direction, may mask significant bias modification effects amongst sub-groups.

4.4.3. ABM-F task engagement and learning optimisation

The main finding when assessing group differences on performance during the ABM-F task was the worsening of performance in the Performance Dependent Feedback group following the early blocks, whereas the Performance Feedback and No Feedback groups

remained consistent across the task. These findings are somewhat in contrast to our prediction that addition of feedback would improve task performance compared to no feedback. The decrease in performance in the Performance Dependent Feedback group may be down to incremental changes in presentation time that were sub-optimal. It should be noted that when developing the task, and testing the increments of change on student volunteers, we settled on a relatively strong increment of change to provoke engagement, which may have been too high for anxious participants, and in fact provoked increased errors. A further explanation is that the stress of the task had a more negative impact on highly anxious participants. As suggested earlier, part of the rationale for increasing task difficulty was that the greater task demand may lead participants to recruit increased voluntary attention and “over-ride” any attentional bias towards task irrelevant stimuli. However, it’s possible that, for those with higher levels of trait anxiety, the greater levels of stress evoked from this increased task demand may have in fact exaggerated their existing attentional biases and thus impeded task performance, i.e. occupying strategic processing and leaving greater influence of automatic threat biases. Alternatively, research has demonstrated that when social anxiety fears are activated prior to attention training this can actually have a positive effect on training outcomes; Kuckertz et al (2014) found that when participants completed an exercise to activate social anxiety fears prior to attention training they reported a greater reduction in attention bias and social anxiety symptoms following training than those completing attention training without fear activation. Theoretically, it is proposed that attention training may be more beneficial with activation of fear schemata, as this provokes the maladaptive attention bias to be ‘active’ and thus more readily targeted (Neubauer et al, 2013). Thus, it appears more research is required in order to establish the specific conditions of state anxiety activation required for a positive effect on training.

Another view is that increasing difficulty based on improved task performance may not be the most optimal approach. Schyner et al (2015) took the opposite approach, by

increasing task difficulty (by adding more distractors compared to target stimuli) in response to a decrease in performance. They found increasing task difficulty when the participants' performance got worse had a beneficial effect on bias modification. They suggest this works by externalising the attentional bias, i.e. making the bias more tangible to the individual, by creating an awareness that they are being distracted by the negative stimuli, and therefore prompting them to focus more readily on the target stimuli. They propose this increase in task difficulty produces an error signal that being distracted by the aversive stimuli is undesirable and makes the task more difficult, thus teaching them to monitor their attentional states more efficiently. However, it is also possible that participants simply needed longer than one session to adjust and improve on this task variant, and that over a longer period, with more accurate incremental change, this may have more effectively optimised learning. In fact, this performance-based method of feedback may have still prompted strong user engagement, however if the task was indeed calibrated to a level that made errors frequent it would have consequently prompted negative performance. In turn, this suggests task performance is not necessarily the best index of user engagement and some users may already be performing at ceiling level. Finally, as this is a relatively simple and repetitive task, expectations of significant improvement in performance, regardless of feedback variation, may have been optimistic. In relation to this, as all participants in this study were tested in a room with a researcher present and minimal distractions, task engagement was likely to be fairly equivalent across conditions. Future research testing how feedback conditions translate to remote ABM use, where task engagement and reduction of distractions may be much more variable and important, could see stronger group differences in performance and modification outcome.

4.4.4. ABM and mood

No differences emerged on the self-report mood measure - the analyses do not show the feedback element prompts either improved positive or reduced negative mood compared

to no feedback. A more overt state anxiety measure (such a stressor task) may have provided more insightful findings. The study design did not allow for any investigation of training effects on trait anxiety, or associations between trait anxiety change and attention bias: training effects on trait anxiety were not investigated as this was only a single session of ABM training, whilst the ‘selected’ nature of the sample meant anxiety differences within the sample were likely too narrow for meaningful correlation analysis between attention measures and symptom severity at baseline.

4.4.5. Limitations

There are a number of limitations to the current study that should be noted. First, the absence of an active control group means that bias changes cannot be attributed directly to the ABM training (above natural variations over time, or simple practice effects from the initial measures). Second, the collection of qualitative feedback of participants’ experience during the task would have been beneficial. This would have provided an alternative and insightful way to evaluate task engagement – particularly with only indirect measures of task engagement available (such as task performance), and just one session of training unable to assess engagement indicators, such as retention rate. Third, in splitting the groups by initial bias and ABM-F group we must interpret the findings with caution, due to the relatively low group sizes and thus low statistical power in some analyses. Fourth, whilst initial bias direction thresholds were based on previous empirical work for the dot probe tasks (Fox et al., 2015; Zvielli, Bernstein, & Koster, 2014), we were unable to find any empirical basis for thresholds in the EVST. We did also run the EVST analysis using a higher confidence criterion of ± 150 ms, and found the same pattern of results, albeit a slightly weaker effect for the no bias group. Finally, as participants were screened and measured using an overall anxiety measure this restricted us from analysing whether direction of initial bias, or patterns of change, was indicative of a specific anxiety sub-group.

4.4.6. Future directions and conclusions

With the possibility that biases in spatial orienting do not uniformly underpin anxiety, tasks such as positive visual search variants, that may more effectively target processes such as cognitive control and goal-directed attention, seem a promising area to develop. Thus, it would be interesting to see how this training approach fared across several trials, in regard to both attention bias and anxiety symptoms. Furthermore, consideration of initial bias direction in future research may provide greater insight into whether this is an important factor in subsequent anxiety changes. Finally, whilst the results demonstrated group allocation to have no effect on bias modification, future approaches could still provide interesting results: further research testing these ABM-F variants outside the laboratory (where the individual must complete the tasks autonomously) and for multiple sessions, along with obtaining qualitative feedback, may provide more insight into the effect of task feedback on motivation and user engagement.

In conclusion, the results suggest that positive visual search training does change the attentional processing of threat related information, however, addition of task feedback has no additional effect after one training session. Bias change does appear to transfer to another measure of attention bias, but only when initial bias direction is taken into account - however it is unclear what this effect can be attributed to. Further research investigating the use of positive visual search variants (such as feedback), aiming to encourage task engagement and optimise learning, may benefit from testing efficacy in remote usage where distractions are likely greater, and over multiple sessions where differences in effectiveness may become more pronounced. Based on the significant effect initial bias direction had on results, future studies could benefit from developing methods to individualise the measurement of changes in attention bias, as the large (and often-found) within-sample variation of attention bias limits the usefulness of a mean bias score.

Chapter 5

5

Boosting emotion regulation in socially anxious adolescents: The use of fMRI-based neurofeedback

Social anxiety is prevalent in adolescence. Avoidance of social situations is a clinical characteristic of social anxiety and may serve to maintain fears. Reducing social avoidance and enhancing exposure to social situations through cognitive reappraisal may be an effective strategy in attenuating social anxiety. Directly targeting the neural substrates of cognitive reappraisal through fMRI-based neurofeedback (NF) may be promising. Here, we used NF to increase ‘adaptive’ patterns of negative connectivity between the dorsolateral prefrontal cortex (DLPFC) and the amygdala to change reappraisal ability, social avoidance and approach behaviours in adolescents. In this study, twenty-seven female participants aged 13-17 years with varying social anxiety levels completed a NF training task in which they were encouraged to practice cognitive reappraisal strategies, whilst receiving real-time feedback of DLPFC-amygdala connectivity. All participants completed experimental measures of social approach-avoidance behaviour and a simple questionnaire measure of cognitive reappraisal before and after NF training. The results demonstrated that an avoidance of happy faces was associated with greater social anxiety pre-training. Participants who were unable to acquire a more negative pattern of connectivity through NF training displayed significantly greater avoidance of happy faces than those who did acquire the more ‘adaptive’ connectivity pattern. These ‘maladaptive’ participants also reported significant decreases in reappraisal ability from pre to post NF. Therefore, NF training may impact social approach-avoidance tendencies in some adolescents. Future research is warranted to develop strategies (and the training parameters) for improving social-approach behaviour amongst young people.

5.1. Introduction

Social anxiety, characterised by persistent fear of negative social evaluation, is common in young people (Knappe, Sasagawa, & Creswell, 2015). Normative social fears and concerns arise with puberty and across adolescence when youth exchanges with peers change both qualitatively and quantitatively (Feldman & Elliott., 1990). Clinically-impairing social anxiety is also often first diagnosed during this transitional period (Beesdo, Knappe, & Pine, 2009). Adolescent social fears include speaking in front of peers, joining groups, speaking with new people, and asking for help at school (Rao et al., 2007; Spence & Rapee, 2016). With increasing levels of social anxiety, young people often choose to avoid these feared situations (Miers, Blöte, Heyne, & Westenberg, 2014; Sumter, Bokhorst, & Westenberg, 2009), which can be detrimental to ongoing academic, personal and social development (Rao et al., 2007; Van Ameringen, Mancini, & Farvolden, 2003). Additionally, avoidance of social situations may maintain social anxiety by preventing any natural extinction of fears that may occur as a result of exposure (McManus, Sacadura, & Clark, 2008). One plausible strategy for managing social anxiety in adolescence could therefore focus on reducing avoidance of, and encouraging approach behaviours towards, social stimuli. This chapter presents a study that uses fMRI-based neurofeedback (NF) on acquiring adaptive patterns of amygdala-DLPFC connectivity to teach more effective cognitive reappraisal strategies and alter social approach-avoidance behaviour.

Throughout development, individuals learn to appraise the social information they encounter, with their appraisal of ambiguous events identified as an important contributor to their ongoing mental health and social functioning (Gross, 2013). Individual differences in this ability emerge in adolescence to influence and regulate emotional responding and subsequent behaviours (Garnefski et al., 2002; Garnefski et al., 2002a; Hofmann, Heering, Sawyer, & Asnaani, 2009). More particularly, maladaptive emotion regulation (ER) strategies have been linked to the maintenance of social anxiety symptoms in adolescents;

one such strategy particularly relevant to the maintenance and reinforcement of social anxiety is behavioural avoidance (Aldao, Nolen-Hoeksema, & Schweizer, 2010). In socially anxious individuals, behavioural avoidance has been identified as a maladaptive coping mechanism for distressing emotions that arise in situations where there is a possibility of negative social evaluation from others (Hofmann, 2007). Whilst avoidance of perceived threat will effectively reduce short-term feelings of anxiety, this behaviour also restricts the opportunity to challenge irrational interpretations of the event. Consequently, the individual may attribute the non-occurrence of feared outcomes to the safety behaviour, and thus strengthen the distorted beliefs (McManus, Sacadura, & Clark, 2008). Experimental tasks have been developed to index socially-avoidant behaviours; the approach-avoidance task (AAT; Rinck & Becker, 2007) has been found to be sensitive to social anxiety differences in adults (Heuer, Rinck & Becker, 2007) but also anxiety differences in adolescents (Klein, Becker, & Rinck, 2011). In brief, the AAT requires the participant to engage in fast approach and avoid actions to social stimuli (emotional faces) via a joystick. Reaction times across different task conditions index the degree to which individuals avoid socially-aversive stimuli and approach socially-appetitive stimuli (Phaf, Mohr, Rotteveel, & Wicherts, 2014). Studies using this task have found socially anxious individuals demonstrated a greater tendency to avoid emotional faces than non-socially-anxious individuals (Heuer, Rinck & Becker, 2007; Roelofs et al., 2010).

Reductions in avoidance behaviours have been shown to be critical to symptom change in social anxiety (Silverman et al. 1999; Williams, 1996), and it is suggested avoidance behaviours can be successfully modified by training adaptive ER strategies (Gross, 2002). One such strategy is cognitive reappraisal; this involves changing the way one appraises the emotional meaning of information (such as a social situation), and thus modifying the intensity of emotion it evokes. Adaptive regulatory responses, such as cognitive reappraisal, can aid in reducing negative emotions evoked from ambiguous or

mildly negative situations and thus consequently reducing subsequent avoidant behaviours as a coping strategy. As outlined in prior chapters, cognitive training techniques have been developed to target dysfunctional appraisals and potentially boost ER in adolescents (Lau, 2013), with some reductions in social avoidance and social anxiety (as per chapter three). However, on the whole results have been mixed (Cristea et al., 2015b) or weak in magnitude (Krebs et al., 2018). In light of these mixed results, alternative methods to boost cognitive reappraisal and reduce socially-avoidant behaviours in adolescents should be explored.

One alternative approach is to more directly boost the neural substrates of cognitive reappraisal. This approach is particularly pertinent to adolescent populations, where brain networks responsible for emotion regulation are thought to be going through a vital period of development (Paus, 2005), and therefore providing an opportunity to cultivate healthy connectivity between brain regions associated with adaptive emotion regulation. Extensive human work suggests that areas of the prefrontal cortex (PFC), and amygdala are heavily implicated in emotion processing and regulation (Hare et al., 2008; Ochsner & Gross, 2005). While the amygdala has been shown to play a key role in fear and salience processing (Adolphs, 2002), regions of the PFC are proposed to have a top-down, regulatory role in relation to amygdala activation in psychiatrically-healthy individuals, serving to reduce affective reactivity and associated stress responses (Banks, Eddy, Angstadt, Nathan, & Phan, 2007; Etkin, Büchel, & Gross, 2015). In particular, negative patterns of connectivity between the DLPFC and amygdala have been demonstrated during tasks involving ER, including cognitive reappraisal (Ochsner, Bunge, Gross, & Gabrieli, 2002). In contrast, weaker negative connectivity between these regions associate with various psychiatric disorders, including anxiety in adults and social anxiety in adolescents (Prater, Hosanagar, Klumpp, Angstadt, & Luan Phan, 2013) (although a somewhat different pattern of perturbations in amygdala-PFC connectivity has sometimes been found in anxious adolescents; Gold et al., 2016). Regardless, boosting stronger patterns of negative connectivity between these regions

that resemble those of psychiatrically-healthy adults (rather than anxious adults) could benefit cognitive reappraisal. Establishing these neurocognitive patterns in adolescence could be more optimal, given that this appears to be a turning point where the nature of connectivity between regions of the PFC and amygdala changes from positive connectivity to the desired negative connectivity as children mature beyond 10 years of age (Gee et al., 2013). Thus, these developmental changes could provide a window of flexibility for learning more adaptive patterns of connectivity to impact cognitive reappraisal (Ahmed, Bittencourt-Hewitt, & Sebastian, 2015; Haller et al., 2016).

In this study, we used a novel brain training approach, real-time fMRI-based neurofeedback (NF), to reinforce these more adaptive patterns of connectivity between the DLPFC and amygdala. NF utilizes the latest developments of real-time data analysis (Johnston et al., 2010) enabling participants to monitor the relevant activity and connectivity of specific brain areas in order to learn to self-regulate their brain responses and therefore emotion regulation strategies (Koush et al., 2015). One study has already shown that children and adolescents can be taught to regulate activity in ER regions (Kadosh et al., 2016); one of the key findings was that the self-regulation effects were not limited to the NF target region, but also had a differential effect on the overall ER network. This demonstrates the suitability of this approach to affect and modulate the underlying networks in the developing brain. In a second study, researchers used functional connectivity-based NF (fc-NF) to directly modulate ER network connectivity in girls aged 14-17 years (Zich et al., 2018). Specifically, they were able to successfully train participants to modulate the functional coupling of the PFC and the amygdala towards a more negative connectivity pattern, which resembles the connectivity pattern found in the mature adaptive/healthy brain, and away from the positive connectivity patterns that predominates in younger children and anxious adults (Gee et al., 2013; Prater et al., 2013), but with individual differences in responsiveness to NF. However, to date no

research has investigated how exactly training adaptive (i.e. more negative) connectivity patterns will affect relevant behaviours outside the scanner, such as social avoidance.

To address this gap, the current study investigates whether the provision of feedback on patterns of connectivity between the amygdala and DLPFC can affect socially-avoidant behaviours in adolescents outside the scanner. Given individual differences in the degree to which these co-activation patterns can respond to neurofeedback (i.e. become more negative), the primary hypothesis is that, amongst those who are responsive to training, there should be a significant reduction in socially-avoidant behaviours, and significant improvement in self-report cognitive reappraisal ability. However, given prior findings of weaker (negative) functional connectivity of the amygdala and DLPFC in socially-anxious youth, we first tested the hypothesis that there would be associations between social anxiety symptoms and socially-avoidant behaviour with these co-activation patterns at baseline.

5.2. Methods and Materials

5.2.1. Participants and procedures

A total of 46 female participants (mean age = 15.09 years; SD = 1.18 years; range 13-17 years) were recruited from local schools in Oxfordshire. 27 of these participants (mean age = 15.22 years; SD = 1.22 years; range 13-17 years) received real-time feedback of negative patterns of functional connectivity between the amygdala and DLPFC. All participants had normal or corrected-to-normal vision and no self-reported history of neurological and psychiatric disorders. This study was approved by the Oxford University Research Ethics Committee. Participants were tested individually. Informed consent and assent were obtained from the primary caregiver and young person respectively before any testing took place. Participants also completed a number of self-report questionnaires on social anxiety and emotion regulation, before completing the AAT. The AAT was completed

in a quiet private room with no distractions. They were then prepared for fMRI scanning and provided with instructions for the in-scanner tasks. Firstly, to identify key emotion regulation regions of the brain to be used in the NF task, a reappraisal task (“localiser”) was conducted inside the scanner. Following this, the NF training was completed. The participant then left the scanner and repeated the AAT, followed by a full debrief. Each participant received a £20 gift voucher for taking part.

5.2.2. Questionnaire measures

Social anxiety (pre-training only)

Social anxiety was measured using the Social Anxiety Scale for Adolescents (SAS-A; La Greca & Lopez, 1998), a 22-item self-report measure of social anxiety symptoms. Participants rate how much they feel each item is true for them (e.g. ‘I worry about doing something new in front of others’) on a 5-point Likert-scale from 0 (not at all) to 5 (all the time). Total scores on this measure can range from 1 to 90. Internal consistency was $\alpha = 0.81$.

Cognitive reappraisal (pre and post-training)

Cognitive reappraisal was measured using items from The Cognitive Emotion Regulation Questionnaire (CERQ; Garnefski & Vivian Kraaij, 2006) assesses 18 emotion regulation strategies including cognitive reappraisal. Items are rated on a 5-point Likert scale ranging from 1 ((almost) never) to 5 ((almost) always). Two items specific to positive reappraisal were used in these analyses: “I think I can learn something from the situation” and “I think that I can become a stronger person as a result of what has happened”, giving total scores ranging from 2 to 10. Internal consistency was $\alpha = 0.73$.

5.2.3. Approach Avoidance Task (pre and post-training)

The AAT (Rinck & Becker, 2007) tests automatic behavioural avoidance tendencies to emotional stimuli (faces) (Figure 5.1). Participants were asked to react to a single picture on the centre of the screen (an adult face with either a happy or angry expression, and a gaze of either straight or averted left/right), by pulling or pushing a joystick (with their dominant hand) in the instructed direction, as quickly and accurately as possible. Upon movement of the joystick, the picture grew or shrunk in size (depending on push or pull) creating the impression of movement towards (approach) or away (avoidance). When the joystick reached 30° in the intended direction the picture disappeared and the joystick had to be returned to the centre position and the ‘fire’ button pressed for the next trial to begin. The task consisted of two blocks of 64 trials (each block preceded by 18 practice trials). In the congruent block, participants were instructed to pull happy faces toward them and push angry faces away, whereas in the incongruent block, participants pushed away happy faces and pulled angry faces towards them. The block order was counterbalanced across participants. Reaction times (RTs) were recorded at four joystick angles (7°, 14°, 21° and 30°). For data analysis, time between stimulus onset and the maximum joystick displacement (30°) was used (Radke, Roelofs, & De Bruijn, 2013). Trials in which participants moved the joystick to maximum joystick displacement in the incorrect direction were recorded as errors.

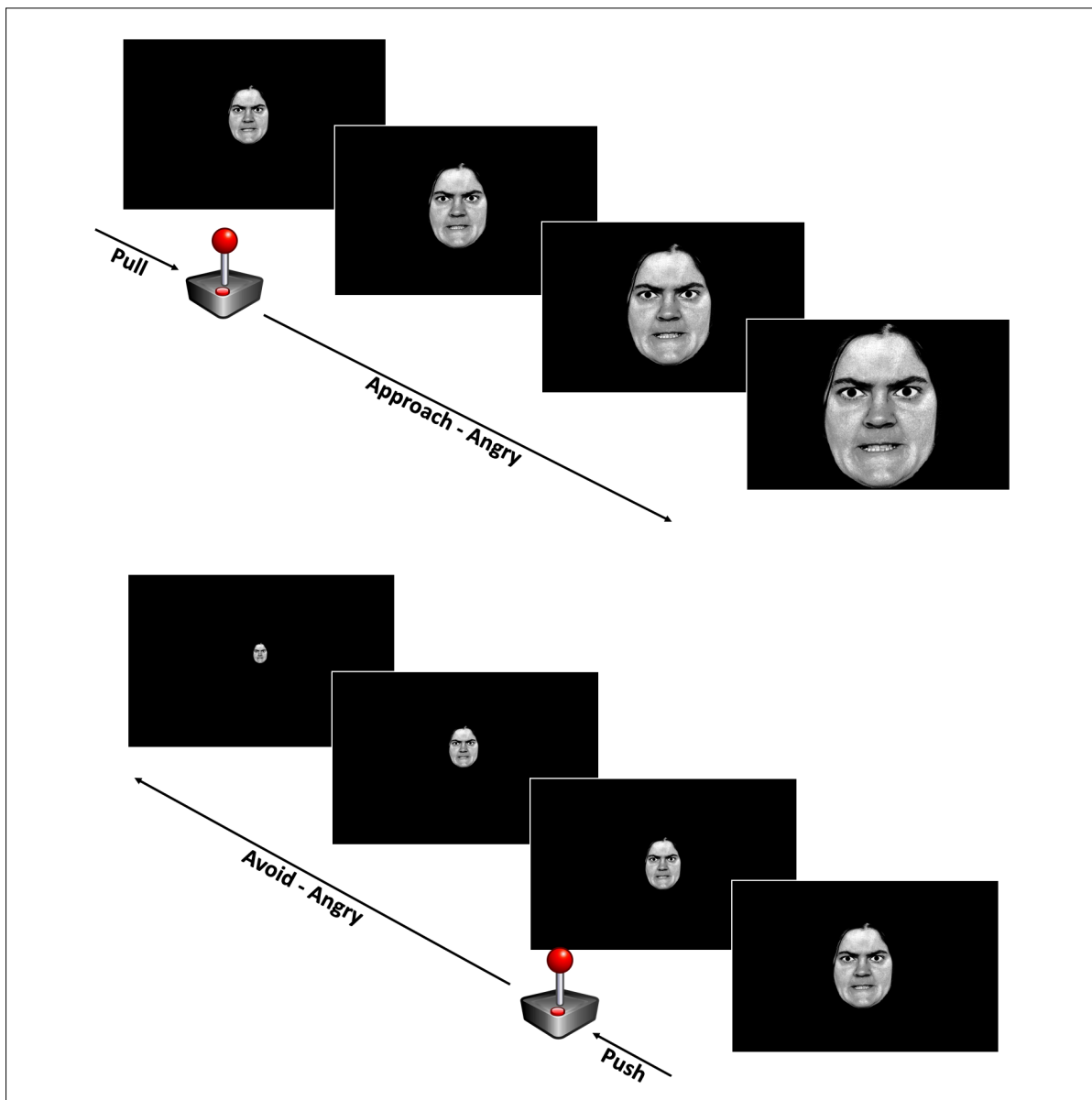


Figure 5.1. Graphic representation of the Approach Avoidance Task with angry faces.

5.2.4 fMRI Tasks

fMRI Image acquisition

FMRI data acquisition was performed using a 3 T Siemens MAGNETOM Prisma MRI scanner (Siemens AG, Erlangen, Germany) using a standard 32-channel head matrix coil. Prior to the functional tasks a high-resolution structural volume was obtained from each subject using a T1-weighted magnetization-prepared rapid-acquisition gradient echo

(MPRAGE) sequence (TR = 1900 ms, TE = 3.97 ms, FoV = 192 x 192 mm², flip angle = 8°, slice thickness = 1 mm, sagittal). Functional measures comprised the localizer task and four NF training runs. The localizer comprised 570, and each NF run 310, 2D multiband gradient echo planar imaging volumes (Todd et al., 2016) (2.0 x 2.0 x 2.0 mm voxels, 0.57 mm gap, TR = 933 ms, TE = 33.40 ms, FoV = 192 x 192 mm², flip angle = 64°, 72 slices, Multi-band factor = 6, fat saturation, transverse slices with phase encoding in the A >> P direction). In order to avoid saturation effects, 10 additional volumes were acquired but not analysed at the beginning of the localizer task and each NF run.

Localiser Task

A reappraisal task (Figure 5.2; Haller et al., 2016) was used in order to provide the individual with cognitive reappraisal strategies and prompt activation of specific brain regions involved in emotion regulation for use in the NF task. During each trial of the task participants were shown a picture of a social scene from the perspective of a female adolescent approaching the scene, depicted from the back. Each scene (lasting 3.73 seconds) connoted themes of negative peer evaluation (appraisal event), which the participant was instructed to appraise freely. Following appraisal, the participant was presented with a positively valanced explanation of the scene (3.73 seconds). Participants were then shown the scene again (3.73 seconds) and asked to attempt to re-interpret it in the direction of the explanation (reappraisal). This was repeated for 30 trials, with an inter-trial interval displaying a fixation cross for 0.93 seconds. The task lasted a total of 9 minutes. Based on the brain activity maps yielded from this task, regions involved in emotion regulation were selected to be used for participant feedback during the NF task.

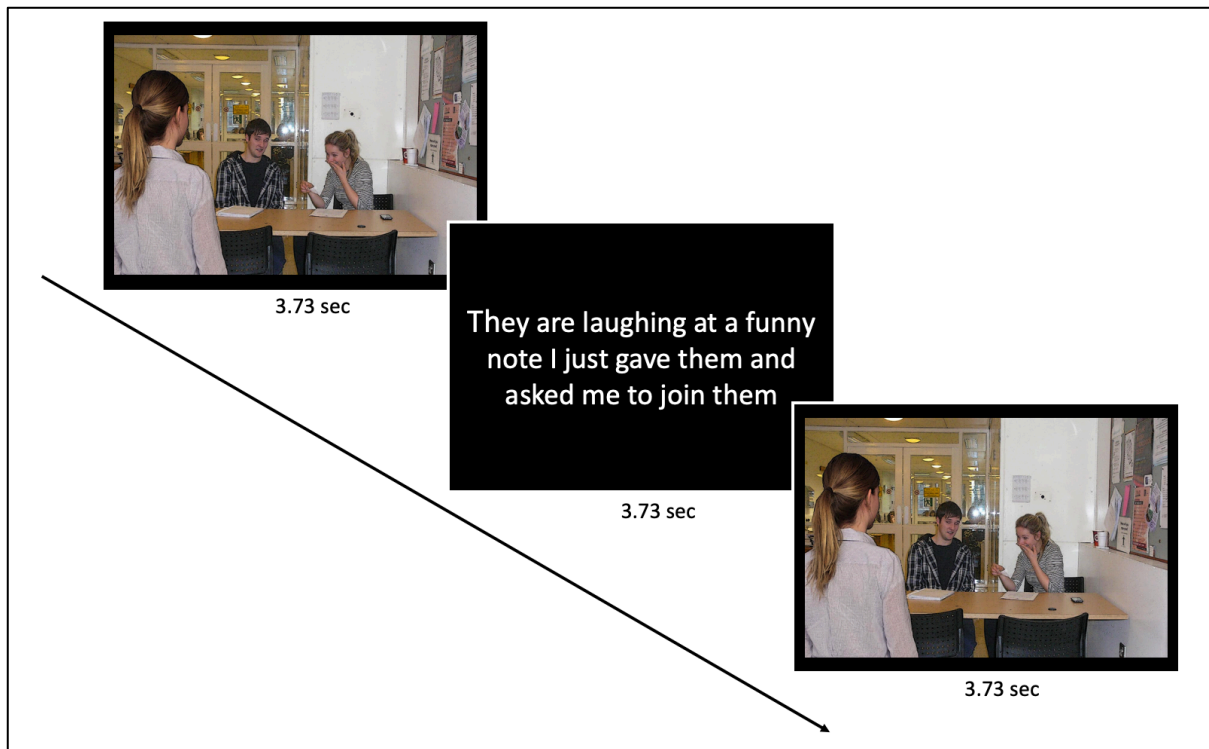


Figure 5.2. Graphic representation of the reappraisal task used to localise ER areas of the brain.

Neurofeedback Training

NF training consisted of four runs, each lasting 4.8 minutes (Figure 5.3). Each run started with a fixation cross in the centre of the screen for 18.66 seconds, which the participant was instructed to focus their attention on. During each run the participant received seven blocks of NF (each lasting 18.66 seconds), during which they saw continuous feedback of brain activity via a simple picture of a '10-point thermometer'. The number of segments filled in provided the participant with real-time indication of the functional-connectivity between the target regions first defined using the localiser task; this was the negative partial correlation between DLPFC and amygdala relative to an unrelated brain region (a white matter region of the left corticospinal tract). Participants were given the following instructions: "You will see a thermometer with a green rim on the screen. The red bars show how much the regions that are important for emotions are active. Your job is to get these regions as active as possible! So, try to get this thermometer up as much as possible. Similar to the task before, try to control your thoughts towards a positive feeling. When the

thermometer does not have a green rim, the thermometer is not working. However, even if the thermometer is not working, your task will be the same and we are still measuring how much your brain is active. The two different thermometers will alternate.” Participants also received seven no-NF blocks in each run, during which participants were asked to continue with the same strategies they were using during the NF blocks, but that the thermometer would be frozen at point six. NF and no-NF blocks were presented in alternating order. To allow participants to differentiate between NF and no-NF blocks, the thermometer in the NF runs was presented with a green frame around it, whereas during the no-NF blocks this frame was missing.

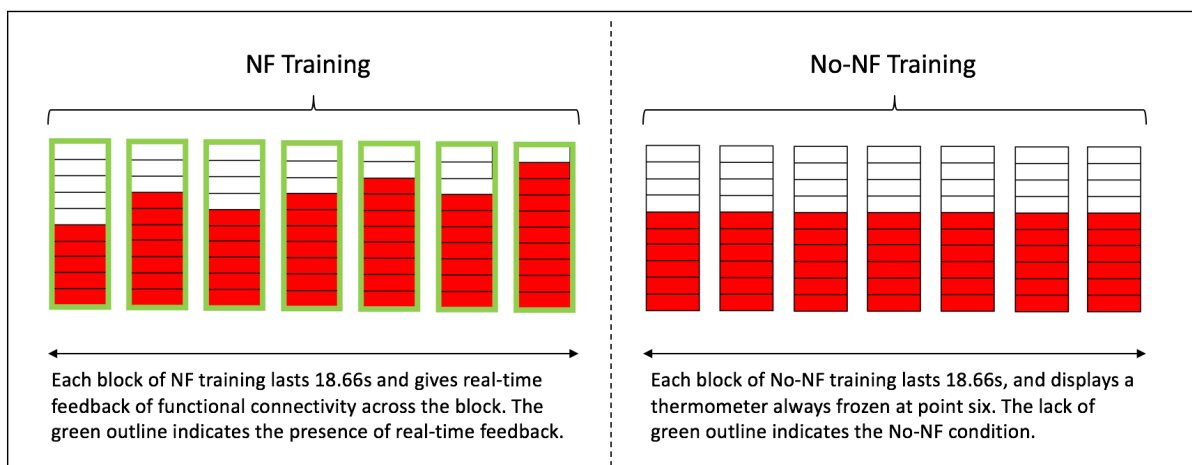


Figure 5.3 Graphic representation of Neurofeedback training.

5.2.5. Statistical analysis plan

Data cleaning and extraction: AAT

As per previous research using the AAT (Enter, Spinhoven, & Roelofs, 2014; Heuer, Rinck, & Becker, 2007; Roelofs et al., 2010), reaction time outliers were filtered using lower and upper cut-offs of 150ms and 1500ms, respectively. Following this, a cut-off of three standard deviations from the mean was used to remove outliers. Incorrect responses were also removed. 91.4% of responses remained, for which medians were calculated per cell (defined

by Emotion, Gaze and Action). No differences between conditions were observed for error rates. As per previous studies (Enter, Spinhoven, & Roelofs, 2014; Heuer, Rinck, & Becker, 2007; Roelofs et al., 2010), effect-scores were calculated as an index of approach/avoidance tendencies. These were calculated by subtracting the mean reaction times for pull movements from the mean RTs for push movements for each emotion per individual. Therefore, negative effect-scores indicate stronger avoidance tendencies and positive effect-scores indicate stronger approach tendencies for each emotion. As there were no significant differences between straight and averted gaze conditions for each Emotion (all t 's < .23, and all p 's > .82), we combined mean RTs for each gaze direction across the Action-Emotion combination.

To measure Cronbach's alpha for the AAT, all trials were combined into pairs based on facial expression. For example, one face-pair would consist of happy-pull male1 and happy-push male1. An effect score was calculated for each face pair and pairs sharing the same emotion were then analysed for internal consistency. Internal consistency of AAT effect scores was $\alpha=0.76$ for angry faces and $\alpha=0.67$ for happy faces.

Data processing: functional connectivity

Initial functional connectivity for each participant was defined as the average partial correlation of the first two blocks of the first NF run (as described in Zich et al., 2018).

To determine which participants were able to acquire an adaptive pattern of connectivity in response to NF training versus those who were not, we used a training direction variable. This was quantified as the slope of the linear regression for average functional connectivity (i.e. the partial correlation between DLPFC and amygdala relative to a white matter region of the left corticospinal tract), from runs 1 to 4 for each participant. Using this slope variable, we divided participants into those who had a gradient of increasingly negative connectivity across runs (average slope = -.023, SD = .019) as those

who were able to acquire an *adaptive* pattern (n=13) and participants who had a gradient of increasingly positive connectivity across runs (average slope = .031, SD = .025) as those who acquired a *maladaptive* pattern (n=14).

Data analysis

To assess the validity of the AAT, we tested whether approach-avoidance tendencies toward each emotion (Angry/Happy), pre-NF, were in the predicted direction. To do this, we conducted a two-way repeated-measures analysis of variance (ANOVA) with Action (Push/Pull) and Emotion (Angry/ Happy) as the within subject variables. Next, we investigated whether these behaviours were associated with social anxiety by calculating correlations between AAT effect scores for each emotion and SAS-A scores at pre-training. To test the hypothesis that there would be associations between social anxiety symptoms and socially-avoidant behaviour with less negative amygdala-DLPFC co-activation patterns, we calculated the correlation between initial functional connectivity (FC) and social anxiety scores and AAT effect scores pre-NF. To evaluate if there was a significant reduction in socially-avoidant behaviours, the effects of training direction group on changes in AAT effect scores were analysed in a 2x2x2 mixed ANOVA, with Time (pre, post) and Emotion (happy, angry) as within-subjects variables and training direction group (adaptive, maladaptive) as the between-subject variable. To examine changes in positive reappraisal from pre to post-NF, depending on training direction group, reappraisal scores at pre and post-NF were analysed with a mixed ANOVA of group direction variable (adaptive, maladaptive) and time (pre, post).

Of note, all analysis conducted on pre-NF variables were done with 45 participants, as one participant was excluded from analysis due to RTs on the AAT deviating over three standard deviations from the group mean. Initial FC data was unable to be collected for 6 participants, therefore all analysis conducted with initial FC was performed with 40

participants. Any analysis assessing changes as a function of NF training were conducted using the 27 participants who received real-time feedback of negative patterns of functional connectivity between the amygdala and DLPFC. The excluded AAT participant was within this group, thus all analysis of NF effects on AAT performance was conducted with 26 participants. In all analyses, alpha was set at .05, and effect sizes are reported as partial eta-squared (η_p^2).

5.3. Results

5.3.1. AAT performance and correlations with social anxiety

Figure 5.4 shows the mean RTs for each emotion-action combination for pre- and post-NF measures for all participants who had available data.

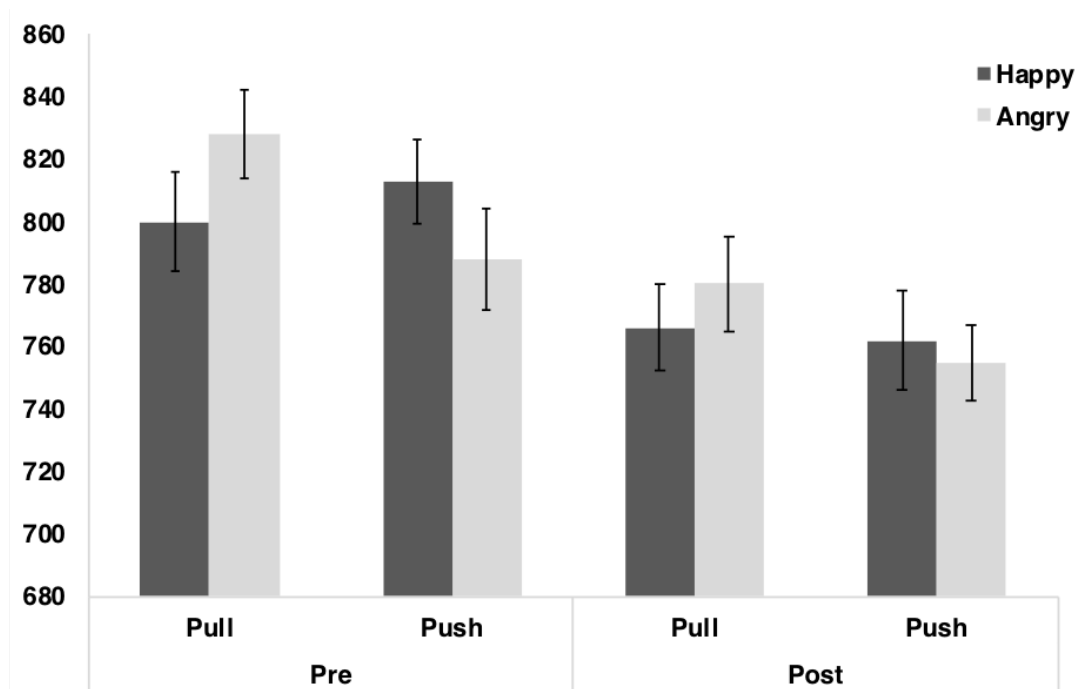


Figure 5.4. Mean reaction times (with standard error bars) as a function of Timepoint (Pre, Post), Picture Type (Happy, Angry), and Response Direction (Pull, Push).

A repeated-measures 2x2 ANOVA with Emotion (Angry and Happy) and Action (Push and Pull) showed no significant main effect of Emotion ($F(1,44)=.102, p=.752, \eta_p^2=.00$), however there was a significant main effect of Action ($F(1,44)=5.92, p=.019, \eta_p^2=.12$), and a significant interaction between the two ($F(1,44)=6.67, p=.013, \eta_p^2=.13$). Decomposing the interaction showed that the extent to which RT scores differed with each action varied depending on the emotion presented. Tests of simple main effects showed that RT means were not significantly different between Happy-Push and Happy-Pull trials ($F(1,44)=1.4, p=.243, \eta_p^2=.03$) but were significantly faster for Angry-Push than Angry-Pull trials ($F(1,44)=10.93, p=.002, \eta_p^2=.20$). Moreover, RT means were faster for Happy-Pull than Angry-Pull trials ($F(1,44)=6.18, p=.017, \eta_p^2=.12$), and also significantly faster for Angry-Push than Happy-Push trials ($F(1,44)=4.45, p=.039, \eta_p^2=.09$).

To investigate the association between social anxiety and social-approach and social-avoidant behaviours, we investigated the correlations between AAT effect scores for each emotion and SAS-A scores at pre-NF. Angry effect scores were not significantly associated with social anxiety ($r(45) = -.07, p = .669$), but happy effect scores were negatively correlated with symptoms ($r(45) = -.33, p = .029$) such that individuals with higher levels of social anxiety were more likely to avoid happy faces.

Table 5.1. Means and standard deviations for questionnaire, fMRI, and AAT measures pre and post NF training.

	Pre		Post	
	N	Mean (SD)	N	Mean (SD)
Initial fc	40	0.28 (0.23)		
SAS-A	45	50.11 (14.18)		
CERQ	44	6.23 (2.22)	40	6.23 (2.26)
Angry Effect	45	-39.73 (80.62)	40	-24.84 (76.52)
Happy Effect	45	13.22 (75.01)	40	-3.63 (79.38)

Note: Initial fc = Initial functional connectivity; SAS-A = Social Anxiety Scale for Adolescents; CERQ = Cognitive Emotion Regulation Questionnaire; Angry Effect = Angry Effect Score for Approach Avoidance Task; Happy Effect = Happy Effect Score for Approach Avoidance Task (negative effect-scores indicate stronger avoidance tendencies).

5.3.2. Correlations between social anxiety and socially-avoidant behaviours, and initial FC

There was a non-significant negative correlation between initial FC and AAT happy effect scores ($r(40) = -.30$, $p = .064$), but a significant positive correlation between initial FC and AAT angry effect scores ($r(40) = .32$, $p = .047$), suggesting that initial FC is more positive in individuals who are more likely to approach angry faces. The correlation between SAS-A score and initial FC was not significant ($r(40) = .19$, $p = .246$). These results also held true for the smaller sample that received NF training.

5.3.3. Pre-to-post NF changes in socially-avoidant behaviour depending on neurofeedback training ability.

A 2x2x2 mixed ANOVA showed a significant 3-way interaction between time, emotion and group ($F(1,24)=8.21$, $p=.009$, $\eta_p^2=.26$). To break down this three-way interaction a Time x Emotion ANOVA was conducted for each group. For the maladaptive

group, neither the main effects of Time or Emotion were significant, however the Time x Emotion interaction was significant ($F(1,12)=4.87, p=.048, \eta_p^2=.29$). To explore this two-way interaction further, we assessed the main effect of time for each emotion: happy effect scores were significantly different pre ($M= 49.46, SD= 70.87$) to post ($M= 3.04, SD= 106.62$) NF training ($F(1,12)=7.01, p=.021, \eta_p^2=.37$), whereas angry effect scores were not significantly different pre ($M= -54.96, SD= 64.28$) to post ($M= -20.69, SD= 107.13$) NF training ($F(1,12)=1.70, p=.22, \eta_p^2=.12$). The direction of these effects suggests that for participants who showed NF change in the maladaptive direction, avoidance of happy faces increased. For the adaptive direction group, there were no main effects of Time ($F(1,12)=0.01, p=.91, \eta_p^2=.00$), Emotion ($F(1,12)=0.18, p=.68, \eta_p^2=.02$) or an interaction effect, $F(1,12)=3.63, p=.16, \eta_p^2=.23$).

5.3.4. Pre-to-post NF changes in self-report positive reappraisal depending on neurofeedback training ability.³

There was a main effect of Time ($F(1,25)=4.75, p=.039, \eta_p^2=.16$), but no significant Time x training direction interaction ($F(1,25)=1.42, p=.245, \eta_p^2=.05$). However, due to a priori expectations around changes in reappraisal, we nonetheless carried out separate paired sample t-tests for each group on the pre and post-NF variables. The reduction in positive appraisal from pre ($M= 6.50, SD= 2.10$) to post ($M= 5.71, SD= 2.37$) in the maladaptive group was significant after correction for multiple comparisons ($t(13)= 2.80, p=.015, d = .53$)

³ As an alternative to categorising participants via their connectivity slope on the NF task, we have also used simple linear regressions to test functional connectivity across the NF task as a continuous predictor of change in outcome measures. This was investigated by creating change scores for each outcome measure, which were each entered into a separate simple linear regression as the dependent variable, with connectivity slope as the predictor variable. For AAT-happy scores, the model was significant ($R^2=0.10, F(1,37)=4.12, p=.05$). It was found connectivity slope significantly predicted change in AAT-happy scores ($\beta_1 = -846.64, p=.05$), suggesting more maladaptive connectivity over NF training predicts increased avoidance of happy faces pre-to-post training. For change in AAT-angry scores the model was not significant ($R^2= 0.095, F(1,37)=3.88, p=.056$). Connectivity slope did not significantly predict change in AAT-angry scores ($\beta_1 = 973.72, p=.056$). Likewise, for change in cognitive re-appraisal the model was not significant ($R^2=0.007, F(1,119)=0.26, p=.611$). Connectivity slope did not significantly predict change in cognitive re-appraisal scores ($\beta_1 = -3.71, p<.611$).

but not amongst the adaptive group (pre: $M= 6.92$, $SD= 2.10$; post: $M= 6.70$, $SD= 1.97$; $t(12)=0.61$, $p=.553$, $d = .24$).

5.4. Discussion

The current study set out to test whether real-time fMRI neurofeedback could be used to target neural correlates of emotion regulation and alter socially avoidant behaviour in unselected adolescents. We assessed whether any improvement in cognitive reappraisal abilities, targeted through neurofeedback of connectivity between the DLPFC and amygdala, would also be observed. Amongst individuals who were unable to acquire an adaptive pattern of connectivity (an increasingly negative connectivity between the DLPFC and amygdala) through NF training, there was an increasing tendency to avoid happy faces from pre to post-NF training. These same participants also showed a significant decrease in self-report positive appraisal ability following NF training. These changes were absent in the group that were able to acquire an adaptive pattern of connectivity. Consistent with prior work, all individuals pulled happy faces faster than angry faces and pushed angry faces faster than happy faces, but there were differences in these social approach-avoidance tendencies amongst individuals with social anxiety: those with higher levels of social anxiety showed greater avoidance of happy faces than those with lower levels. Finally, initial positive functional connectivity between the amygdala and DLPFC was associated with the tendency to approach angry faces (though not with social anxiety). Each of these findings is discussed in turn.

First, the findings show that in individuals who do not acquire an adaptive pattern of connectivity through NF training, socially avoidant behaviour becomes more pronounced. Furthermore, acquisition of a more “maladaptive” pattern of connectivity through NF training seemed to result in more exaggerated reduction in positive reappraisal ability. These results fall in line with studies showing that an absence of the “adaptive” connectivity is correlated

with social anxiety disorder in adult populations (Kim et al., 2011). Whilst our results did not specifically show improvement of avoidant behaviour in the “adaptive” group, they do demonstrate that those who were able to effectively utilise the training did not show the increase in avoidant behaviour and decrease in self-report reappraisal ability seen in those who were unable to effectively utilise the training. It may be the case that with further development of this relatively exploratory training technique, possibly administered over multiple sessions, we could see positive changes in cognitive reappraisal, reductions in withdrawal behaviour and increases in approach behaviour. However, it should certainly be noted that the increase in avoidant tendencies amongst the group that acquired a more “maladaptive” pattern of connectivity illustrates a potentially aversive consequence of failing to engage with the NF technique. Indeed, we must be mindful that if NF training was conducted over multiple sessions this aversive effect could be further exaggerated for some individuals. This suggests future research should first focus on the salient factors differentiating responders and non-responders in order to ensure training approaches can be adapted to benefit as many individuals as possible and ensure those who may experience adverse outcomes can be readily identified. Whilst the results may indicate that four runs were too few for some participants to identify/consolidate an effective reappraisal strategy (and as such they were left with ineffective strategies, or frustration, resulting in the observed reduction in positive appraisal ability), there may be other psychological variables that differ between responders and non-responders. Based on the current findings, further research investigating the factors that modulate effective upregulation (and positive/negative outcomes) is certainly warranted.

Second, perhaps due to the non-clinical nature of the sample, it appears socially avoidant behaviours manifested not as an avoidance of angry faces (as found in some literature comparing high and low anxious groups; Roelofs et al., 2010), but of positive faces only. Evolutionary-based avoidance tendency for angry faces appear to exist in all individuals

regardless of anxiety levels (Marsh, Ambady, & Kleck, 2005), however, due to the nature of social anxiety - where anxious individuals are excessively concerned about negative social evaluation - differences in avoidant behaviour may have only become apparent when presented with happy faces, due to the distinct lack of threat interpretation to these stimuli by healthy individuals compared with anxious individuals. There is previous evidence that anxious individuals avoid happy faces, at both automatic and controlled levels of processing (Heuer et al., 2007; Mansell, Clark, Ehlers, & Chen, 1999). Finally, when investigating how initial connectivity may impact existing approach-avoidance behaviours, we found a greater likelihood to approach angry faces in those individuals with a ‘maladaptive’ pattern of connectivity between DLPFC and amygdala. This unexpected finding may signal a maladaptive tendency that could be linked to other behavioural problems such as aggression, though without these measures, we were unable to assess this.

There are some limitations that should be noted. Firstly, we did not know whether participants were deploying reappraisal ability during NF training. Although we measured CERQ before and after, we only used a short-form of the CERQ and were therefore only able to base our measure of changes in positive reappraisal on two items from this questionnaire. Future research using the full questionnaire, and/or a specific reappraisal task, may allow us to more accurately determine whether associated changes in approach-avoidant behaviour and functional connectivity through NF training were related to changes in cognitive reappraisal ability. Second, the effects of only one session of NF training were assessed. Multisession training may allow individuals to practice and consolidate more effective and robust reappraisal strategies, which may have had larger effects on social avoidance and possibly, symptom change too; however, the aversive effect of training in some individuals must be taken into account when considering a multi-session approach. Third, we used an all-female sample - this was to limit homogeneity in the sample given many age and gender effects in adolescence. Fourth, the modest sample size in each group may have limited the

significance of some statistical comparisons. Finally, whilst the AAT task has been shown to associate with social anxiety symptoms, it is not necessarily an ecologically valid test of behavioural avoidance as a maladaptive safety behaviour.

In conclusion, this study has demonstrated that in our non-clinical sample of female adolescents, socially avoidant behaviour of positive faces was associated with greater social anxiety. When using neurofeedback training to alter cognitive reappraisal, we found that those who were unable to acquire a more 'mature' and adaptive pattern of connectivity showed increased avoidance of happy faces and decrease in positive appraisal ability. These results suggest that NF training can have a differential effect on cognitive reappraisal ability and subsequent social approach-avoidance tendencies, however, at present this effect is not in the desired direction. Further research is required to understand factors differentiating individuals who show an aversive reaction to training and those who do not, and identify the optimal parameters for positive outcomes.

Chapter 6

6

Discussion

6.1 Overview

This thesis focused on evaluation of methods to enhance the modification of anxiety-linked cognitive biases in adolescents, and assessment of the expression of attention bias in anxious young people. This final chapter will first summarise the findings from each empirical chapter, before presenting general limitations that should be considered when interpreting these findings. Subsequently, I will present discussion of the overall findings and potential future directions for the methods evaluated, before presenting final conclusions.

6.2 Summary of studies

Preceding the three experimental studies, *chapter two* aimed to address inconsistent results from RT measures of attention bias. Results from studies investigating attention bias in anxious young people using RT tasks have been highly variable. As eye-tracking has now been employed in enough studies of anxious youth to warrant effect size compilation, I conducted a meta-analysis to evaluate whether this measure can provide a more convincing/accurate indication of whether children and adolescents are characterised by vigilance (initial fixation) toward threat, as is reported in adult RT and ET studies. This also provided the opportunity to assess other expressions of attention bias that may characterise anxious youth; therefore, chapter two also used a meta-analysis to investigate whether anxiety in youth is characterised by maintained attention towards threat, i.e. do anxious youth more often dwell upon threatening stimuli versus non-threatening stimuli across the whole trial, compared to non-anxious youth? The results indicated there was no absolute vigilance bias (a bias score significantly different from zero) in anxious or non-anxious youth. There

was also no significant difference in vigilance between these groups, and relatively low heterogeneity of variance in effect sizes. Nevertheless, a-priori moderator analyses were run on between-group differences with no significant moderators identified. The second meta-analysis evaluating between-group effects of maintained attention did reach significance; a small effect was found, demonstrating greater avoidance of threat over the entire viewing period in anxious compared to non-anxious youth. Moderator results found a significant influence of type of anxiety group used; studies including a mixture of anxiety types showed greater between-group effect sizes than those using only social anxiety. Due to mixture of diagnoses in the mixed group, including social anxiety, this was not a clear-cut finding.

In the first of the three experimental studies, *chapter three* employed a case series design to investigate the effectiveness of a newly developed ‘enhanced’ CBM program that aimed to target biases of attention, interpretation and attribution, over multiple sessions of training, in nineteen 16-18yr olds with elevated levels of social anxiety. This study aimed to build upon previous ABM/CBM-I findings by incorporating several features identified in the literature as having potential to improve efficacy of CBM. Firstly, multiple biases were targeted, based upon the combined bias hypothesis: attention bias was targeted using a dot probe task (one session with word stimuli, and one session with face stimuli), and two variations of a visual search task; the first using a 3x3 grid of faces, and the second aiming to improve real-life generalisability by using pictures of visual social scenes, as well as incorporating questions to encourage recognition of internally focused attention. Interpretation bias was targeted using several variations of ambiguous situations tasks. Firstly, a ‘standard’ version, using linguistic stimuli; secondly, adapting this task to utilise visual representations of ambiguous scenes; finally, adding questions to each of these to modify biased internal attributions of negative interpretations. This study measured attention and interpretation biases using the dot probe task and adolescent interpretation bias task (AIBT), respectively. Symptoms were assessed using the SAS-A, SCARED, MFQ, and a

new ‘diary’ measure of social interactions through the week - designed to improve ecological validity of symptom measures. The program showed good acceptability, with a high completion rate. Compared to changes over the baseline period, changes pre- to post-CBM training showed significantly greater reduction of social anxiety symptoms (on SAS-A) and socially-avoidant behaviour (on the ‘diary measure’). There were also reductions of depressive symptoms and general anxiety symptoms. Bias modification effects were mixed; post-hoc tests did show a significant change in interpretation bias; however, this was seemingly weak. There was, however, a significant association between this change and symptom reduction on SAS-A. There was no change in attention bias, very poor test-retest reliability of the dot probe (RT) measure, and negative qualitative feedback regarding the ABM aspect of the study.

Chapters 4 and 5 aimed to build upon existing area of improvement identified for cognitive training approaches, that were further compounded by quantitative and qualitative results and from *chapter three*. Specifically, these two chapters aimed to improve efficacy of cognitive training approaches with the use of real-time feedback for attention bias and emotion regulation training. **Chapter four** aimed to address inconsistent modification outcomes from existing ABM approaches by evaluating the addition of two ‘feedback’ elements centred around real-time task performance. The first ‘ABM-F’ task provided explicit performance feedback at the end of each block of positive visual search training, giving the participant information of their average speed across the block and its comparison to the previous block. The second ABM-F condition gave an implicit (performance dependent) form of feedback in which the task was made more difficult (in order to retain engagement), by reducing stimulus display time of the positive visual search trials, if the participant met specific performance conditions in the prior block. These conditions were compared to a positive visual search task with no feedback. Pre and post-training measures of attention bias on dot probe and EVST, and positive/negative mood measures were recorded,

as well performance across the ABM-F task. Individual differences in direction of attention bias at baseline were also calculated and its influence on attentional change was assessed. Irrespective of ABM-F condition, significant bias change was found on the EVST measure, but not the dot probe measures, or the mood measures. There was no effect of ABM-F group on any pre-to-post outcomes, however level of performance across the ABM-F task decreased in the performance dependent feedback group. When categorising participants by initial bias direction, those with an initial bias toward threat showed a reduction in this bias on all attention tasks. Those with an initial bias away from threat also showed a change on dot probe tasks, but in the opposite direction than trained. Having no bias at baseline resulted in a change in the trained direction on the EVST and no change on the dot probe tasks. There was no interaction with ABM-F group and no changes in mood.

Chapter five aimed to boost cognitive reappraisal ability by more directly targeting the underlying neural correlates of emotion regulation using real-time neurofeedback of connectivity between emotion regulation areas of the brain whilst positive reappraisal strategies were practiced. It was hoped that by providing real-time reinforcement of successful reappraisal strategies, and providing a task element that was novel and engaging, the individual would more readily identify and consolidate adaptive techniques, leading to positive behavioural change. This study sought to use an alternative approach to self-report measures in testing symptom outcomes by using an approach-avoidance task to experimentally measure social-avoidant behaviours before and after the neurofeedback training. Prior to NF training we measured the strength (and direction) of connectivity between the two identified brain regions at baseline, as well as self-report social anxiety (SAS-A). Before and after the NF training we measured cognitive reappraisal ability using a short form of the CERQ, and approach-avoidant behaviours using the AAT. We found that individuals with greater levels of social anxiety were more likely to avoid happy faces than those with less severe symptoms. We also found that individuals who were able to

successfully utilise the training showed no change in approach-avoidant behaviour, or self-report reappraisal ability; however, those who were unable to upregulate this network of brain regions showed an increased avoidance of happy faces and reduced self-report cognitive reappraisal ability.

6.3. General Limitations

Whilst study-specific limitations have been highlighted within the individual chapters, the following section will discuss further limitations that apply to the thesis as a whole.

6.3.1. Self-report anxiety in community samples

Screening and assessment of all participants in this thesis used self-report questionnaire measures in community samples. Whilst chapters three and four both screened for individuals only with elevated levels of anxiety, it is still possible these individuals do not have the severity of symptoms found in those with diagnosed anxiety disorders, and therefore would not reach diagnostic threshold. Thus, findings can only be firmly generalised to non-clinically anxious youth. Reliance on self-report measures may have also increased susceptibility to demand effects and social desirability – particularly in *chapter three*, which relied upon self-report measures for assessment of symptom change. Validity of self-report measures could have been improved with multi-informant approaches, including parent/teacher and/or clinical diagnostic assessment.

6.3.2. Lab-based measures of dependent variables

A second limitation of all experimental chapters was the reliance on lab-based measures of dependent variables of biases and symptomatic behaviours. This limits the generalisability of findings to ‘real-world’ environments. Only one measure – the diary measure in *chapter three* – was completed outside the laboratory in response to real-world

interactions and did provide some significant results. It may be the case that naturalistic measures record genuine responses and behaviours that are unable to be provoked in artificial settings. Incorporation of further measures such as this, perhaps with incorporation of technology (for instance a smartphone app that allows for easy capture of everyday emotional and behavioural factors), could be beneficial in future research.

6.3.3 Lack of follow-up measures

The single time-point (immediately following the final, or only, training session) of post-training assessments was also a limitation. As learning may take time to consolidate (Abend et al., 2014) and changes in behavioural, psychological and cognitive factors may take time to develop following training (Schmidt et al, 2009), more measures at further time-points would have been beneficial. Relatedly, given the uncertainty regarding the moderating effect of age on cognitive biases in youth, future longitudinal studies investigating bias changes across longer developmental periods, would allow us to better understand the trajectory of these cognitive biases and associations with other developmental changes and anxiety onset.

6.3.4. Control groups

None of the three experimental studies employed a control condition. This puts a limit on what we can infer from the findings. A case series design was decided upon for *chapter three* due to the feasibility nature of the program and the desire to provide the program to as many eligible participants as possible. Whilst the baseline condition allowed for comparison against natural changes across time, we are unable to rule out placebo or demand effects. This is particularly pertinent as the study relied on self-report outcome measures and was advertised as a cognitive training programme for anxious adolescents. *Chapter four* was designed in order to specifically investigate the effects of ABM with feedback compared to

without and therefore the ‘no-feedback’ group was seen as the ‘control group’; however, with inconsistent efficacy of all ABM approaches in the extant literature, a control condition of non-ABM training would have helped identify genuine task affects over and above natural changes across time, and allowed for investigation of the potential ‘regression to the mean’ effect when evaluating the impact of initial bias direction. As it stands, results must be interpreted with this caveat in mind. An active control group for *chapter five* provided a more challenging proposition – previous studies employing active control groups by using “sham feedback” which presents brain activity from non-task-related brain regions (deCharms et al., 2005; Zotev et al., 2011) have raised questions regarding ethical implications (Kadosh, Lisk, & Lau, 2016): providing inconsistent feedback when participants may be using a successful adaptive ER strategy may lead them to discarding it as unsuccessful. As the aim of this chapter was to compare those who could and could not achieve successful brain connectivity, it was decided no control group was necessary. However, a non-active control group could have still provided a beneficial comparison for behavioural and self-report changes pre- to post-training.

6.3.5. Gender

It should be noted that the gender distribution for *chapters three and four* were strongly skewed towards female. In *chapter five* we only recruited female participants to control for variance due to potential effects of gender on development of the studied brain areas (Giedd et al., 1996; Reiss, Abrams, Singer, Ross, & Denckla, 1996). Whilst gender disparity is not uncommon for studies of adolescent anxiety, it is a factor that must be considered in terms of generalisability of findings.

6.4. Discussion of findings

This section will first present several pertinent implications arising from the study of attention bias and appraisal biases before focusing upon how the various methodological features implemented to boost cognitive training could be improved for future training approaches.

6.4.1. Implications for theory

Attention Bias

General consideration of findings

Chapters three and four both attempted to boost positive outcomes from ABM training. Where *chapter three* aimed for reduction in social anxiety symptoms and bias change by using a combination of ABM dot probe and visual search approaches, alongside CBM-I in a multi-session package, *chapter four* added different forms of feedback in an attempt to more effectively modify attention bias in one session. Both chapters found no overall effect of ABM training on attention bias when evaluated using the dot probe task. However, *chapter four* did see an overall change in attention bias using the EVST measure. There could be several interpretations of these outcomes:

One possible explanation for the lack of training effects on automatic attention bias to threat across both studies is the poor reliability of the dot probe task (Waechter et al., 2014) – it is possible that there were training effects, however due to a high amount of random measurement error these changes were not observed. If this is the case, due to our reliance on the dot probe task as the sole attention measure in *chapter three*, it also limits our understanding of any genuine effect attention training may have had on symptom reduction effects. Alternatively, it could be argued that there was no change in automatic attention

orienting - interpreting modification outcomes in light of the meta-analysis results from *chapter two* suggest that if an automatic orienting bias toward threat does not characterise anxiety in youth, then the dot probe results are less surprising. Moreover, where *Chapter four* found an improvement in bias scores as measured by the EVST, it is potentially because these tasks measure somewhat differing attentional processes; the dot probe task showing stimulus very briefly and thus measuring stimulus-driven attentional deployment, but the EVST displaying stimulus for a longer period and requiring active search, thus tapping into more strategic top-down attentional processes. If this is the case, it could also be proposed that attentional change may have been achieved in *chapter three* (which also included two sessions of positive search training) but the dot probe task at 500ms was unable to identify this. Additionally, it could be suggested that due to the differences between dot probe and EVST tasks (such as number of stimuli, task action, presentation time, and task-relevant instructions) more extensive training is required for any attentional change to generalise to such between tasks. Of course, it cannot be discounted that as the EVST uses the same task action as the positive search training tasks, changes may have been task-specific practice effects rather than any genuine change in attentional processing.

A final important factor regarding our consideration of ABM results is the wide variability in the direction of attention bias at baseline, demonstrated in *Chapter four*. When using composite scores, as many RT measures do, this can result in a bias score of almost zero when averaged across the sample. It could be argued that if there are sample sub-groups of individuals particularly suitable for, and beneficial of, a specific training approach this variation may lead to dilution of effects when collapsed across the sample. Thus, individuals in *chapter three* that did benefit from the attention training may have been missed.

Thus, the results from attempts to boost ABM provide a mixed impression. Overall, they demonstrate a lack of success in boosting attention bias modification, but also illustrate

the need for reliable measures of attention bias, in order to accurately and reliably capture attentional change outside task practice effects.

Theoretical considerations for future directions

One consideration when developing further research is our conceptualisation of attention bias. *Chapter two* focused upon how measurement approaches of attention bias in youth anxiety, alternative to RT, could give greater insight into how we conceptualise attention bias as a characteristic of youth anxiety; however, measurement of attention from other chapters also contribute to discussion of this area. The results from the meta-analysis in *chapter two* do not indicate a uniform attention bias in (overt) attentional orienting toward threat amongst all youth, as found in adult studies, but do highlight the potential influence of strategic avoidance (potentially as a maladaptive emotion regulation strategy). However, a lack of reliability from first fixation measures (Waechter et al., 2014; Wermes et al., 2017), the relatively broad picture of any patterns of attention across time provided by mean dwell time measures, and the likely moderating influence of multiple situational and dispositional factors makes identification of stable attentional markers of ‘youth anxiety’ as a whole particularly difficult. Indeed, results from *chapter four* demonstrates the variability that can exist within a sample and, moving forward, it appears important to recognise that attention bias toward threat does not appear a robust characteristic of all anxious youth, but instead may characterise just a sub-set of individuals - it may be that expression of attention bias toward and away from threat varies between individuals as a function of multiple factors which require identification through tightly controlled research studies, with reliable attention measures.

In fact, interpreting current results in synthesis with the extant literature could even suggest that current conceptualisations of attention bias as linear expressions toward/away from threat do not accurately portray the complexity of attention bias in anxious youth. It

could instead be suggested that biases in attention are likely the transient result of multiple influences differing within and between individuals, and as such a static score is unable to take into account variability in attention bias, which leads to inconsistent results. Zvielli et al (2015) have created a method to operationalise the variability as an index of attention bias. They calculate trial-level bias scores (TL-BS) to provide an index of average and peak positive and negative attention biases, but also a score indicating the level of attentional variability across time. Advancements in measurement, such as this, which expand not only how we measure existing constructs but also how we advance existing conceptualisations, may help provide more reliable indices of attention bias. Indeed, further development of attention measurement using approaches such as eye-tracking (Chen et al, 2015; Eckstein, Guerra-Carrillo, Singley, & Bunge, 2017), and ERP (Bunford, Kujawa, Fitzgerald, Monk, & Phan, 2018; Thai, Taber-Thomas, & Pérez-Edgar, 2016) to advance existing attention bias constructs may also allow us to identify unique attentional signatures that more accurately predict variance in youth anxiety symptoms.

Thus, current findings suggest that targeting specific components of attention will potentially only provide suitable training for a sub-section of most samples, unless accurate predictors of stable attentional expression have been identified. In turn, this suggests some focus of future ABM research should be on development of ABM methods with broader approaches that are more inclusive of the variability we see in attention bias expression and provide greater consideration of strategic influence. For instance, recent formulations (Mogg & Bradley, 2018; Waters & Craske, 2016) suggests anxious youth develop maladaptive attentional regulation, resulting in excessive threat monitoring or avoidance (as demonstrated by rapidly fluctuating attention bias between and within individuals; Zvielli, Bernstein, & Koster, 2014) and biased threat evaluation (Waters & Craske, 2016). Thus, if it is the case that attention bias in anxious youth is highly variable in its expression, then developing training that targets processes underlying attentional control may be the preferable direction

for future research (e.g. Sanchez, Everaert, & Koster, 2016). The positive visual search task utilised in *chapters three and four* was selected due to its suggested wider suitability in this sense and, with the above factors in mind, still appears to provide a suitable option for further development. Building upon this approach to develop more overarching training tasks that target dysfunctional processes involved in varying expressions of attention bias, with repeated practice targeting both effortful and automatic processes, could provide improved outcomes. Discussion of how methodological features of training approaches utilised in this thesis may inform further development of ABM, in synthesis with the above implications, is presented in section 6.4.4.

Appraisal biases

General consideration of findings

Chapters three and five attempted to boost the modification of appraisal processes. Specifically, *chapter three* attempted to use CBM-I with task additions, such as images of social scenes and incorporation of attribution training, in an attempt to implicitly adjust the meaning attached to emotionally ambiguous situations, whereas *chapter five* attempted to provide real-time feedback of regulatory brain activity in order to facilitate effective practice of explicit emotion regulation strategies based on a previously completed reappraisal task. Results from *chapters three and five* suggest that the methods employed to train more adaptive appraisals both provide some promise - we saw significant change in both studies. Importantly, we found that changes in interpretation bias did correlate with symptom reduction in *chapter three*, and successful engagement with NF protected against increased avoidant behaviour in *chapter five*. However, the results of *chapter three* showed that despite post-hoc analyses indicating a significant reduction in interpretation bias scores pre- to post-training (and no significant change pre to post baseline phase), there was an absence of a

significant interaction effect between phase and time in the repeated measures ANOVA, suggesting that the degree of change between baseline and training phases wasn't significantly different. Furthermore, when inspecting the individual scores, it became apparent that some individuals experienced strong significant change, whereas others none at all. Similarly, the results from *chapter five* indicate that around half the participants did not respond to NF training in the desired way.

Interpreting these findings alongside the ABM results, this again suggests that there may be some individuals suitable for these training approaches and some that are not – and there may be specific factors that predict effective training response. These results provide several points of discussion.

Theoretical considerations for future directions

The NF results give neurobiological evidence that those with weaker ability to upregulate emotion regulation networks of the brain have significantly worse outcomes following explicit ER training using NF; i.e. greater avoidant behaviour. Interpreting these results from a dual-process perspective (which proposes adverse behavioural outcomes are the result of an imbalance between an automatic impulsive system and a controlled reflective system; Strack & Deutsch, 2004) suggests that for unsuccessful participants control capacity remains low and thus the reflective system is unable to override automatic impulse-triggered behaviours, meaning subsequent overt behaviours, such as approach-avoidance, are more likely to reflect the influence of automatic processes. The results from NF training suggest that individuals who cannot successfully engage in the NF task may in fact decrease motivation to subsequently engage in regulatory control, resulting in increased (maladaptive) impulsive response. In turn, this suggests that these participants could benefit more (or additionally) from CBM-I to implicitly modify learned associations that connect the stimulus (potential social interaction) to the automatic safety response (avoidance). In fact, there is

research suggesting adolescents with worse regulatory control (who also had the most negative interpretation bias) benefit most from CBM-I training (Salemink & Wiers, 2012). Of course, these results also suggest there are improvements to be made with NF tasks in order to facilitate reappraisal improvements in more individuals (see section 6.4.4.); however, incorporation of CBM-I approaches with NF could provide interesting results. Furthermore, due to exaggerated individual differences at this relatively volatile period of development, more research utilising fMRI methods with these methods could identify neurobiological markers that predict training suitability for specific methods (Lueken et al., 2016).

A further salient point from these results is that our findings do not indicate the mechanism of change for those who did benefit from CBM-I training. Whilst the aim of CBM-I was to train new automatic processing of ambiguity, when inspecting the qualitative feedback from *chapter three*, several of the participants indicated they found the interpretation training aspect helpful as it “allowed them to see situations more realistically/positively”. In turn, this raises the question of whether the mechanism underlying improvement is in fact automatic or whether it may actually be more closely related to the use of effortful emotion regulation strategies, such as reappraisal. It is possible that some participants developed both effortful emotion regulation strategies (potentially due to increased insight and understanding the goal of the task) as well as changes in automatic interpretation of situations through continued task practice. In fact, it may be the case that understanding of the training goals itself boosts modification; providing more explicit instructions regarding the goal of the task could aid in the development of effective effortful strategies that may become habitual with continued use (Gyurak, Gross, & Etkin, 2011), as well as modifying automatic processing bias through task practice.

Our inability to disentangle the potential mechanisms of change does highlight an important limitation; the lack of ‘online’ measures of interpretation bias means we cannot be sure whether observed change in elaborative interpretations translates to automaticity. The

incorporation of both offline and online tasks, such as lexical decision tasks or incidental learning tasks (Hazlett-Stevens & Borkovec 2004; Khatibi et al., 2014; Vancleef et al., 2009), would be beneficial in future research to help us understand whether training effects on effortful processing has translated to automatic processing for both CBM-I and NF training. In fact, completion of cognitive and behavioural measures inside the scanner could help assess whether reductions in social-avoidant behaviour following cognitive training does emanate from increased top-down inhibitory control of emotional reactivity, and whether during increased stress or cognitive load automatic response bias is still reduced following training (i.e. transfer to automaticity), and how the neural underpinnings of that response differ.

Therefore, multi-session CBM-I and NF training have both demonstrated potential to have some impact upon appraisal processes and social anxiety symptoms, though findings have been mixed, with some aversive outcomes. Current findings are unable to fully disentangle whether these methods have an effect on automatic or effortful processes. The use of experimental re-appraisal tasks and online/offline interpretation tasks in future research, in combination with neuroimaging, would help assess the underlying mechanisms of symptom reduction following cognitive training. Furthermore, current results suggest certain individuals may be more/less responsive to specific training approaches, therefore further research to identify cognitive and neurobiological markers for treatment suitability will provide beneficial insights for training development.

Combined bias considerations

Targeting biases in combination in *chapter three* was designed due to the possibility of it strengthening the effect of cognitive training. However, the design didn't allow for assessment of the relative or interaction effects of each approach (ABM/CBM-I) other than with correlation analysis following completion of all training. Recent research studies have

found a reciprocal link between reappraisal and attentional deployment; a recent study by Kim, Kim, and Kim (2016) found that successful reappraisal training was linked with reduced task-irrelevant attention bias to negative information. In a study using gaze-contingent attention control training, Sanchez et al (2016) found that training increased attentional control, led to negative attention bias reduction and greater reappraisal ability on an emotion regulation task via its impact on interpretation bias. Thus, with evidence providing direct and indirect links between attentional deployment, interpretation bias and ER, and the conceptual overlap between CBM-I and reappraisal, there is potential that reappraisal may be a common link mediating the outcome of both attention and interpretation training, in subsequent response to threat. Further research incorporating combined CBM and reappraisal (and other ER) measures, to assess interplay among these cognitive biases, ER, and anxiety symptoms, could provide insightful results.

6.4.2. Implications for training

A prominent axis of this thesis was the evaluation of methodological adjustments to cognitive training tasks for anxious adolescents, with the aim of boosting positive outcomes. Thus, task features warrant discussion regarding how they may inform future investigations.

Task difficulty. This may have had an effect on task performance and engagement, and also provides an interesting avenue for further adjustments. Evaluation of performance (as measured by RT) across the ABM-F task in *chapter four* may have been affected by the relative simplicity of the task, meaning participants were already close to ceiling level relatively early on, and thus improvement in performance across time remained stable regardless of possible boosts in task engagement and motivation by explicit feedback. However, where attempts were made to increase difficulty, by reducing display time, only performance reduction was observed. If the participant was already operating at ceiling level on the variable that was altered this is unsurprising. It's possible that improving difficulty in

other ways will have a more positive effect on outcome; such as increasing the number of distractors based on performance. Furthermore, adjusting task difficulty could also be applied to CBM-I; gradually increasing task demands, such as cognitive load, may keep the individual engaged and may also increase the need for automatic processing to be employed. In NF training it appeared task difficulty hampered some individuals; amending the fMRI feedback weighting values to more clearly show smaller levels of improvement, may improve future engagement and performance.

Explicit vs implicit instructions. As mentioned briefly above, the type of instruction given to the individual may affect task performance and outcome. Whilst CBM training was originally designed to operate as an implicit intervention (to directly modify processes outside conscious awareness through repeated exposure to training contingencies hidden within the task structure), it has also been suggested a clear rationale is required for improved task engagement (Beard, 2011). Some studies employing explicit information regarding training contingencies have shown positive outcomes and increased learning during training (Lazarov, Abend, Seidner, Pine, & Bar-Haim, 2017b; Mobini et al., 2014). Instructions provided to participants in *chapters three and four* were designed as only enough instruction to carry out the tasks correctly in order to keep training contingencies implicit (hidden) and reduce the chance of demand effects; where *chapter five* provided more explicit information regarding training contingencies, but less so about the overall goal of the study. Providing specific instructions regarding training contingencies, task goals, or program objectives may all have potentially boosted effects on bias modification and symptom outcome. Future research is required in order to evaluate which types of information are most beneficial in boosting training effects.

Real-time Feedback. The quality of information provided also extends to feedback. Adjustment of the type of feedback provided in cognitive training tasks may help address issues of more broadly targeting goal-directed control. The ABM-F task in *chapter four*

provided explicit feedback regarding performance, but not in relation to the overarching goals of the task or cognitive processes being targeted. Whilst this may have had no differential effect regarding training performance over one session, it might when further developing the ABM-F task to test impact on symptom outcomes: providing more relevant goal-directed feedback (e.g. emphasising control of attention and reducing distraction by irrelevant anxiety-provoking stimuli), that could prompt greater awareness of goals and self-regulatory control of attention, and be generalised to habitual strategic processing outside the laboratory (in addition to the repetitive task practice to reinforce automatic attention tendencies), may have greater effects on symptom outcomes (e.g. Bernstein et al, 2014; Sanchez et al., 2016). NF training in *Chapter five* did provide more explicit goal-directed feedback to participants, with explicit indication of brain activity responsible for helping them regulate emotions. Whilst this was successfully acquired for over half of the participants, the remaining participants failed to successfully upregulate their ER network and showed a negative change on subsequent outcome measures. Although this may be related to several factors, it is possible the feedback was not useful enough in aiding individuals who were unable to successfully obtain the desired direction of connectivity. It's possible utilising more structured guidance through the task in response to poor performance may keep motivation high and provide greater improvement in some participants.

Training structure. The number of sessions and structure of training may have impacted upon the results found in all experimental chapters. A prominent motivation in the design of the CBM program in *chapter three* was the use of a multi-session approach to target multiple biases during prolonged training. Previous research has indicated more sessions may be important for symptom change (Hallion & Ruscio, 2011). However, the multitude of different modification tasks utilised over the eight sessions of training, may have resulted in a dilution of the specific modification effects as not all tasks may have been suitable for all participants. Future research could attempt to personalise training further by

having a broad range of available tasks from which a more concise selection can be made, based on pre-training assessment, to provide training that most effectively targets specific processes important for the individual (though this relies on accurate measures). Furthermore, it's still relatively unknown what the ideal spacing of training is, however eight sessions over two weeks may have been too condensed and thus inhibited effective consolidation of learning between sessions (Abend et al., 2014). The use of just one session in *chapters four and five* may have also impacted upon outcome. It is possible that group differences in *chapter four* could have emerged after multiple training sessions, and due to the relatively difficult learning curve in *chapter five* more sessions may have been required in order to effectively utilise the NF technique for more individuals. Recent ABM research has shown that learning continued to improve up until the fifth session, after which point it levels off (Abend et al, 2018b), suggesting these tasks may have given more insight into differential rates of learning each technique (and consequences on outcome) over more sessions. Therefore, further research with these tasks requires consideration of optimal number and structure of training sessions.

Content specificity. One approach we took to individualising training more effectively was by presenting stimuli relevant to the individuals' primary anxiety concern (social anxiety in *chapters three and five*); *chapter three and five* attempted to use ambiguous social scenes in order to provide a more immersive depiction of anxiety-provoking situations relevant to socially anxious individuals. It's possible (and likely from the qualitative feedback of *chapter three*) that these scenes were not specific enough to the individuals to provide the strength of outcome we aimed for. It's possible that providing stimuli more personal to the individual would provide a stronger outcome (Pergamin-Hight et al., 2015). For instance, basing scene selection on answers to a pre-training questionnaire filled out by participants, or incorporating specific details into ambiguous vignettes. Furthermore, personalised stimuli that closely mimics personal real-world situations may lead to increased stress and provoke

greater automaticity in cognitive processing, possibly improving the chance of successfully modifying these processes (Hoppitt et al, 2014; Krahé, Mathews, Whyte, & Hirsch, 2016). This is a suggestion that can be carried over to all cognitive training approaches employed; for instance, in ABM-F developments using social scenes of varying difficulty with personal, symptom specific, and goal-relevant information may also improve performance and outcome on ABM tasks.

Combined approaches. To build upon the combined bias approach, targeting more than one bias within each task may provide a greater chance of task suitability for each individual and potentially prompt greater interaction between biases. If the separation of tasks to train attention and interpretation in the ‘combined approach’ of *chapter three* diluted the effect somewhat; incorporation of multiple methods into one task could provide a more consistent outcome. However, it should also be noted that symptom severity at baseline in *chapter three* was not significantly associated with any of the cognitive bias measures. Furthermore, the relatively weak effects on symptoms found from CBM interventions, such as *chapter three*, and the relatively weak association between cognitive processes and symptom change, raises questions regarding how great a role they play in anxiety. Research suggests there are many pathways to anxiety (Vasey & Dadds, 2001) and cognitive biases may potentially play just a minor role in some individuals. Therefore, a future avenue may be immersion/combination of improved CBM approaches with other training packages such as CBT in an attempt to provide a greater chance of successful outcome (Shechner et al., 2014).

6.4.6. Conclusions

This thesis aimed to investigate newly adapted approaches to cognitive training, designed to more effectively target cognitive biases implicated in child and adolescent anxiety. It also evaluated evidence from eye-tracking measures of attention bias in anxious youth. Collation and analysis of eye-tracking results displayed a small significant effect,

indicating a tendency for overall attentional avoidance of threat in anxious youth; but these results also highlighted the need for further research into specific factors affecting individual differences in attention bias and its expression across time increments.

Combined CBM, and task individualisation, showed some potential in symptom reduction; however, these approaches would benefit from further research to identify individual differences in cognitive bias profiles and improvement in reliability of cognitive bias measures. Identifying common processes that underlie cognitive biases and symptom change would aid future CBM development: future combined bias research investigating the interplay between cognitive biases, reappraisal and anxiety symptoms in youth may provide insightful results regarding pathways to change.

Real-time feedback at the neural level provides an innovative opportunity to meaningfully incorporate cognitive neuroscience findings into cognitive training approaches. This approach has potential to improve adaptive emotion regulation at important developmental timepoints; however, it is first important to understand who may be most suitable for this approach and how this approach can be optimised to ensure non-aversive outcomes for all individuals. Behavioural performance-related feedback also has scope for further development in training attention and interpretation; testing over multiple sessions and adapting feedback style and task parameters could improve outcomes.

Therefore, with further advancements in task effectiveness and applicability, CBM approaches still have potential to positively impact upon child and adolescent anxiety.

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Appendices

A

Forest Plots for Chapter Two

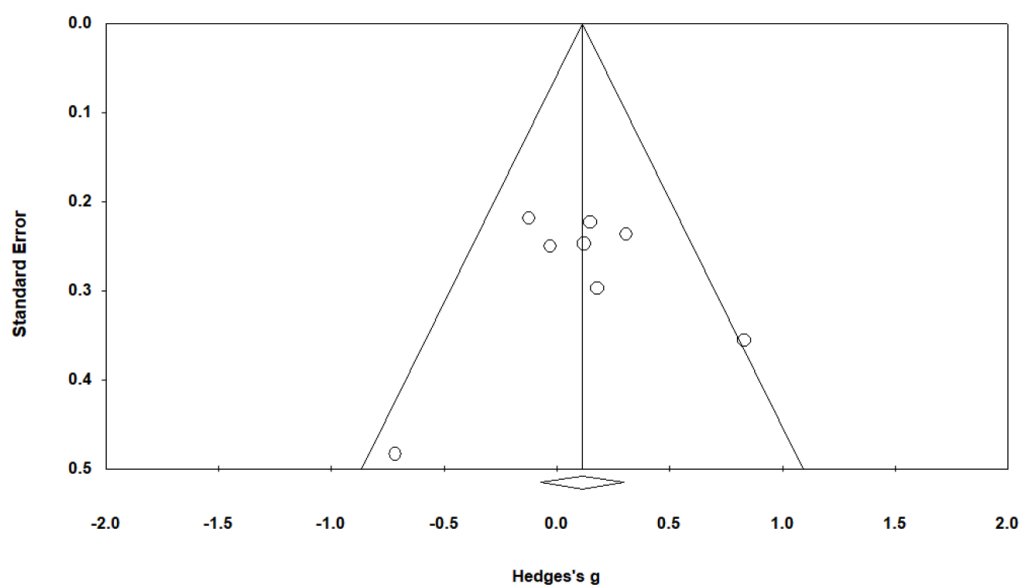


Figure A1. Funnel plot for between-group vigilance analysis

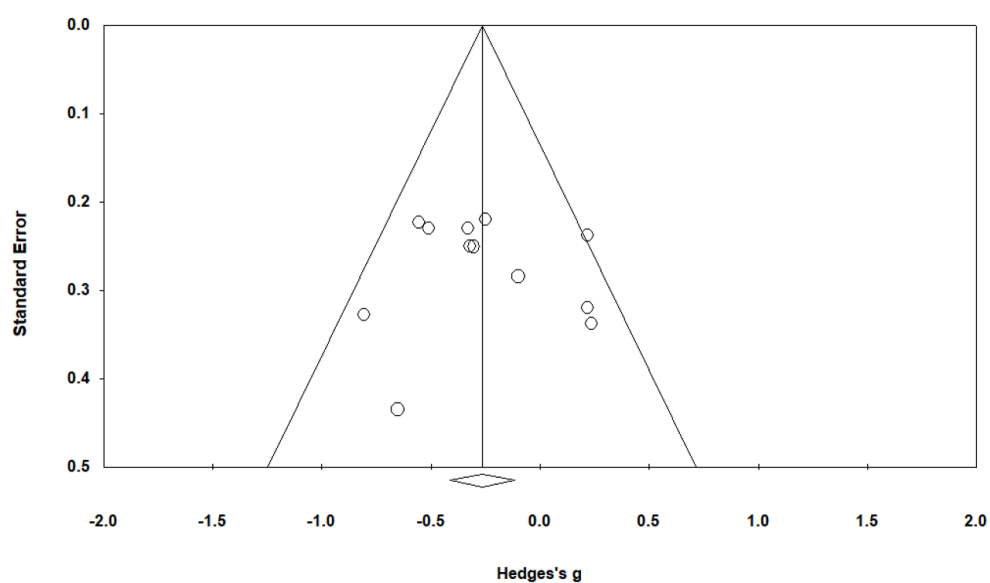


Figure A2. Funnel plot for between-group maintenance analysis

B

Effect of Threat Emotion in Chapter Four

Effect of threat emotion on initial attention bias and change in bias pre to post-training

To assess whether the use of angry or disgust threat faces yielded differential results in initial attention biases measures, independent samples t-tests were run for each attention measure.

The results indicated there were no between group differences for angry vs disgust faces on the EVST, $t(120) = -0.72, p = .474$, the dot probe (neutral-threat), $t(133) = -0.72, p = .473$, and the dot probe (happy-threat), $t(133) = -0.50, p = .620$.

To assess whether angry or disgust faces yielded differential pre to post changes from attention bias modification, a 2x2 ANOVA was run for each attention measure, with Time (Pre, Post) as the within subjects factor, and Emotion (Angry, Disgust), as the between-subjects variable. For the EVST there was a significant main effect of Time, $F(1, 119) = 19.25, p < .001, \eta^2 = .14$, but no significant effect of Emotion, $F(1, 119) = 1.12, p = .28, \eta^2 = .01$, and no significant Time x Emotion interaction, $F(1, 119) = 0.11, p = .744, \eta^2 = .00$. For the dot probe (neutral-threat) task there was no significant main effect of Time, $F(1, 129) = 0.81, p = .776, \eta^2 = .00$, or Emotion, $F(1, 129) = 1.56, p = .210, \eta^2 = .01$, and no significant Time x Emotion interaction, $F(1, 129) = 0.04, p = .850, \eta^2 = .00$. For the dot probe (happy-threat) task there was no significant main effect of Time, $F(1, 129) = 1.07, p = .30, \eta^2 = .01$, or Emotion, $F(1, 129) = 0.01, p = .945, \eta^2 = .01$, and no significant Time x Emotion interaction, $F(1, 129) = 0.84, p = .360, \eta^2 = .01$.

C

Extra Tables for Chapter Four

Table A1. EVST Bias Scores pre- and post-training, by initial bias direction.

Feedback Group	Initial Bias Direction	N	Mean (SD)	Mean (SD)
			Pre-training	Post-training
All	All	121	55.6 (789.48)	-277.6 (649.65)
	No Bias	34	37.2 (132.51)	-241.6 (620.22)
	Bias Toward Threat	44	871.3 (437.02)	3 (607.98)
	Bias Away From Threat	43	-764.5 (430.93)	-593.3 (582.74)
Performance Feedback	All	41	101.4 (779)	-232.2 (636.13)
	No Bias	9	62.1 (145.41)	-258.5 (431.19)
	Bias Toward Threat	16	896.8 (459.26)	81.6 (552.3)
	Bias Away From Threat	16	-672 (287.01)	-531.2 (688.52)
Performance Dependent Feedback	All	39	-110 (801.11)	-318.8 (820.29)
	No Bias	12	38.3 (135.77)	-144.9 (890.27)
	Bias Toward Threat	12	73.82 (479.48)	1.61 (916.5)
	Bias Away From Threat	15	-907.2 (480.08)	-725.9 (493.97)
No Feedback	All	41	167.4 (132.51)	-283.9 (620.22)
	No Bias	13	18.8 (128.31)	-319.1 (437.37)
	Bias Toward Threat	16	945.6 (383.71)	-85.6 (351.46)
	Bias Away From Threat	12	-709.4 (509.78)	-510.3 (549.98)

Table A2. Dot Probe (Happy-Threat) Bias Scores (ms) pre- and post-training, by initial bias direction.

Feedback Group	Initial Bias Direction	N	Mean (SD)	Mean (SD)
			Pre-training	Post-training
All	All	127	-3.7 (49.37)	2.6 (38.6)
	No Bias	66	0.6 (13.79)	4.3 (39.48)
	Bias Toward Threat	26	60.1 (34.54)	3.3 (44.38)
	Bias Away From Threat	35	-59.1 (38.57)	-1 (32.75)
Performance Feedback	All	45	-16.3 (59.42)	10.4 (32.96)
	No Bias	24	-0.1 (15.09)	11.1 (33.48)
	Bias Toward Threat	6	72.3 (29.93)	11.9 (37.12)
	Bias Away From Threat	15	-77.6 (50.63)	8.8 (32.82)
Performance Dependent Feedback	All	40	4.9 (41.13)	0 (36.14)
	No Bias	20	0 (14.37)	-5.6 (33.48)
	Bias Toward Threat	11	5.4 (33.37)	0.7 (51.27)
	Bias Away From Threat	9	-44.4 (15.96)	3.7 (16.03)
No Feedback	All	42	1.7 (13.79)	-3.2 (39.48)
	No Bias	22	1.9 (12.24)	5.8 (49.35)
	Bias Toward Threat	9	59.3 (40.16)	-7 (42.6)
	Bias Away From Threat	11	-45.9 (19.07)	-18.2 (37.99)

Table A3. Dot Probe (Neutral-Threat) Bias Scores pre- and post-training, by initial bias direction.

Feedback Group	Initial Bias Direction	N	Mean (SD)	Mean (SD)
			Pre-training	Post-training
All	All	127	-4 (56.35)	-1.4 (46.24)
	No Bias	57	-0.9 (14.12)	-8.7 (49.4)
	Bias Toward Threat	31	62.8 (39.97)	11.4 (44.78)
	Bias Away From Threat	39	-61.5 (43.83)	-0.8 (41.17)
Performance Feedback	All	45	-3.8 (60.01)	-5.7 (48.97)
	No Bias	21	-2.7 (13.6)	-29.3 (46.76)
	Bias Toward Threat	12	60.3 (38.59)	16.8 (49.23)
	Bias Away From Threat	12	-70 (57.54)	13 (34.59)
Performance Dependent Feedback	All	40	-7.4 (34.72)	0 (39.23)
	No Bias	22	1.8 (15.01)	7.3 (34.2)
	Bias Toward Threat	5	4.92 (17.61)	-1 (26.7)
	Bias Away From Threat	13	-44.7 (20.57)	-8.4 (50.01)
No Feedback	All	42	-0.8 (14.12)	2 (49.4)
	No Bias	14	-2.4 (13.8)	-2.9 (64.09)
	Bias Toward Threat	14	69.9 (46.9)	14.4 (46.3)
	Bias Away From Threat	14	-69.8 (44.73)	-5.6 (37.1)

D

Extra Graphs for Chapter Four

Training performance across task for each condition

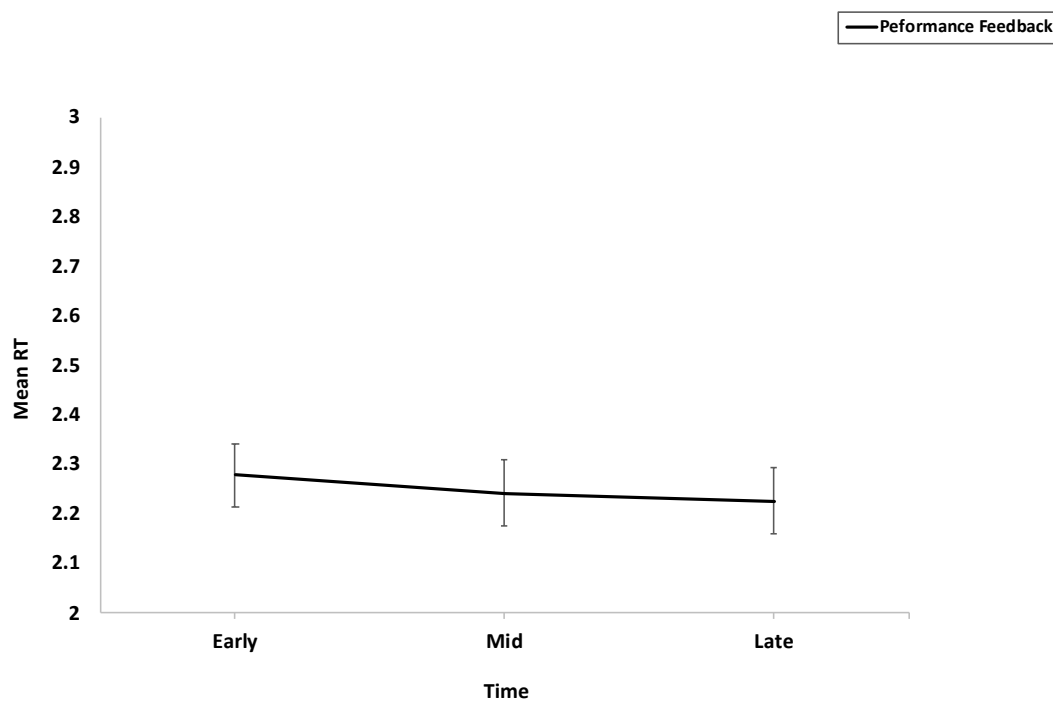


Figure A3. Mean ABM-F reaction time for performance feedback condition as a function of Time-point and Group.

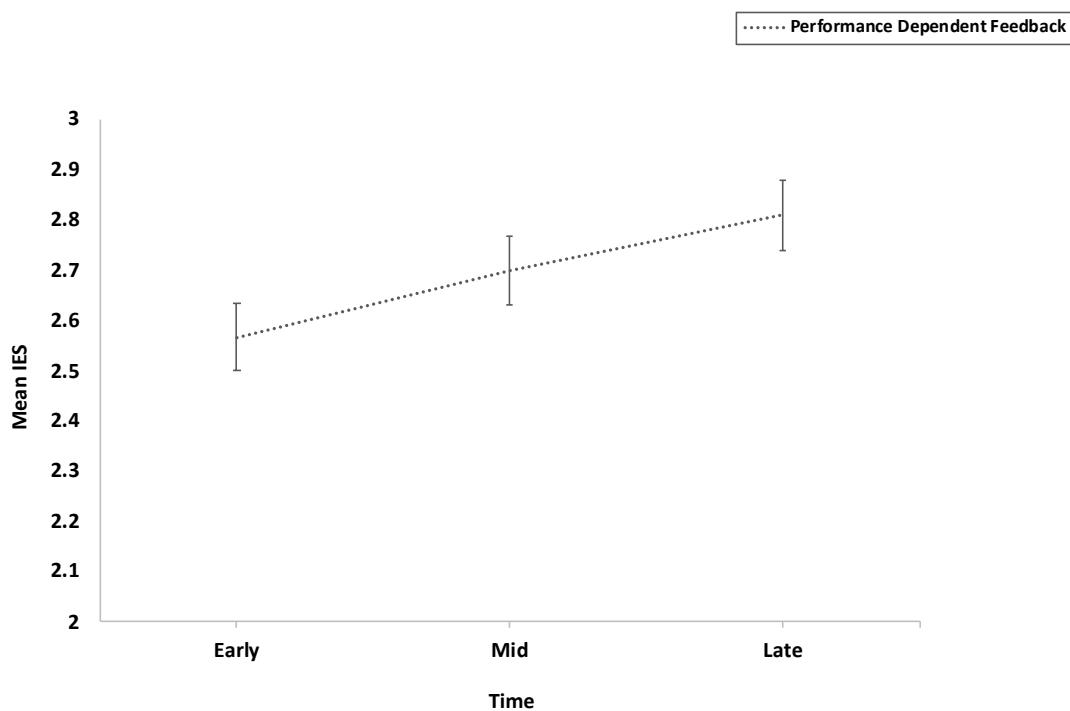


Figure A4. Mean ABM-F Inverse Efficiency Score for performance dependent feedback condition as a function of Time-point and Group.

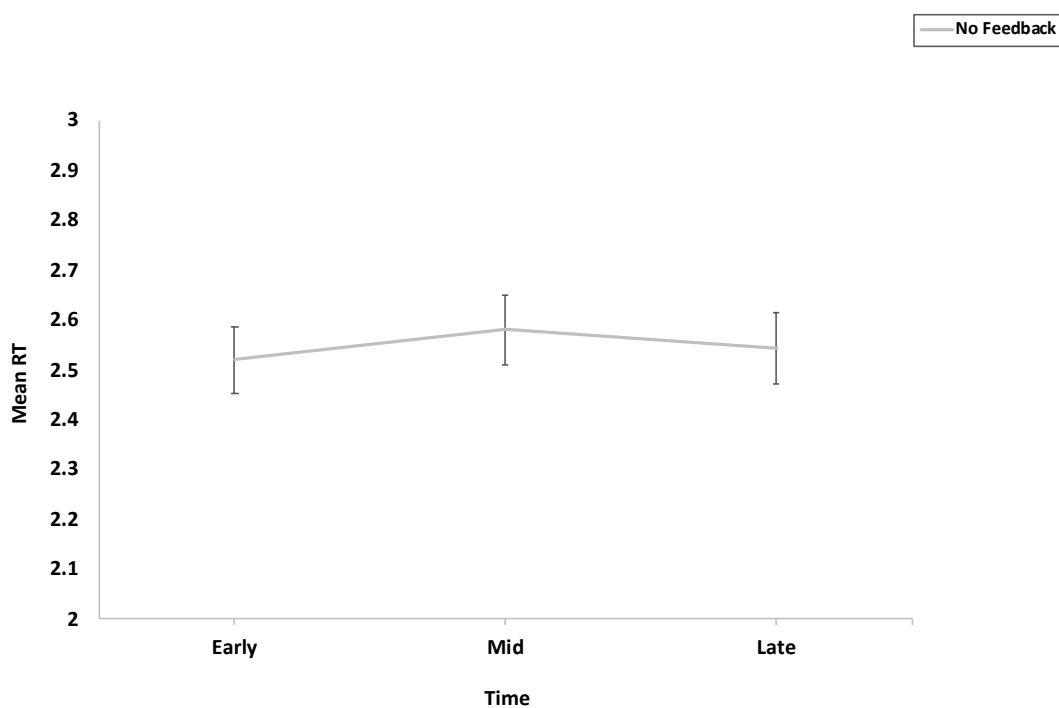


Figure A5. Mean ABM-F reaction time for no-feedback condition as a function of Time-point and Group.